Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting information:

Synthesis of C6”-modified α-*C*-GalCer analogues

General methods and procedures for the synthesis of **7-10**, **12-22**

Precoated Macherey-Nagel SIL G/UV254 plates were used for TLC, and spots were examined under UV light at 254 nm and further visualized by sulfuric acid-anisaldehyde spray or by spraying with a solution of $(NH_4)_6Mo_7O_{24}.4H_2O$ (25 g/L) and $(NH_4)_4Ce(SO_4)_4.2H_2O$ (10 g/L) in H_2SO_4 (10%) followed by charring. Column chromatography was performed on Biosolve silica gel (32 - 63 µm, 60 Å). NMR spectra were obtained with a Varian Mercury 300 Spectrometer. Chemical shifts are given in ppm (d) relative to the residual solvent signals, in the case of $CDCl_3$: δ= 7.26 ppm for ^1H and δ = 77.4 ppm for ^{13}C and in the case of pyridine-d_5: δ = 8.74, 7.58 and 7.22 ppm for ^1H and δ = 149.9, 135.5 and 123.5 ppm for ^{13}C. Exact mass measurements were performed on a Waters LCT Premier XE TOF equipped with an electrospray ionization interface and coupled to a Waters Alliance HPLC system. Samples were infused in a in a CH_3CN/HCOOH (1000:1) mixture at 10 mL/min.

Methyl 2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranose (7)

To a solution of methyl α-D-galactopyranose (5 g, 25.75 mmol) in anhydrous DMF (100 mL) at 0 °C, was added NaH (2.97g, 123.58 mmol) and the reaction mixture was stirred for 30 minutes. Next benzyl bromide (14.78 mL, 123.58 mmol) was added dropwise and the mixture was allowed to reach room temperature and was stirred overnight. The mixture was then cooled to 0 °C and quenched by addition of H_2O (50 mL). The aqueous layer was extracted with EtOAc (3 x 75 mL), the combined organic layers washed with H_2O and brine, dried with $MgSO_4$ and filtered. The organics were removed under reduced pressure and the residue was purified by column chromatography (hexane/EtOAc: 85/15) to furnish galactoside **7** (13.52g, 95%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ 3.35 (s, 3 H, OCH_3) 3.52 (d, J = 6.4 Hz, 2 H, CH_2-6) 3.86 – 3.93 (m, 3 H, H-3, H-4 and H-5) 4.01 – 4.07 (m, 1 H, H-2) 4.35-4.97 (m, 9 H, $\underline{CH_2}$Ph and H-1) 7.19 – 7.43 (m, 20 H, $CH_2\underline{Ph}$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.33, 69.07, 69.22, 73.27, 73.46, 73.55,74.72 ,75.17, 76.45, 76.58, 77.00, 77.21, 77.43, 79.11, 98.79, 127.46, 127.54, 127.65, 127.67, 127.73, 127.91, 128.07, 128.19, 128.23, 128.30, 128.34, 128.36, 137.97, 138.51, 138.64, 138.82; Exact mass (ESI-MS) for $C_{35}H_{38}KO_6$ $[M+K]^+$ found, 593.2315; calcd, 593.2305.

1-allenyl-6-O-acetyl-2,3,4-tri-*O*-benzyl-α-D-galactopyranose (8)

To a solution of methyl 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranose (5.7 g, 10.28 mmol) in anhydrous acetonitrile (30 mL) at 0 °C, was added propargyltrimethylsilane (80 – 90%, 3.85 mL, 20.55 mmol) followed by the addition of TMSOTf (1.37 mL, 5.14 mmol). The reaction mixture was stirred for 2 days at 0 °C and upon disappearance of the starting material (as judged by TLC), Ac_2O (15 mL) was added dropwise. The mixture was allowed to stir for another 30 minutes at 0 °C before addition of DCM (100 mL) and saturated $NaHCO_3$ solution (50 mL) to quench the reaction. The aqueous layer was extracted with DCM (2 x 75 mL) and the combined organic layers were washed with brine, dried with $MgSO_4$ and filtered. The organics were removed under reduced pressure and the residue was purified by flash column chromatography (20 → 30% EtOAc in hexanes) to furnish allenyl-sugar **8** (3.49 g, 66% over 2 steps) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ 2.02 (s, 3 H, CH_3) 3.73 (dd, J = 8.5 and 2.8 Hz, 1 H, H-4) 3.93 (t, J = 2.7 Hz, 1 H, H-3) 4.02 – 4.09 (m, 2 H, H-2 and H-5) 4.17 (dd, J = 11.7 and 4.1 Hz, 1 H, Ha-6) 4.27 – 4.36 (m, 1 H, Hb-6) 4.60 – 4.89 (m, 9 H, H-1, $\underline{CH_2}$Ph, CH=C=$\underline{CH_2}$) 5.41 (td, J = 6.7 and 5.0 Hz, 1 H, $\underline{CH}$=C=CH_2) 7.29 – 7.40 (m, 15 H, $CH_2\underline{Ph}$); Exact mass (ESI-MS) for $C_{32}H_{34}NaO_6$ $[M+Na]^+$ found, 537.2245; calcd, 537.2248.
Spectral data are consistent with the literature data.
[1]

1-allenyl-6-O-p-methoxybenzyl-2,3,4-tri-*O*-benzyl-α-D-galactopyranose (9)

A solution of allene **8** (4.42 g, 8.6 mmol) in a 7 N NH_3 in methanol solution (80 mL) was stirred for 3 days at room temperature. Upon deacetylation the solvents were removed under reduced pressure and the residue was used without further purification.
The crude sugar was dissolved in anhydrous DMF (30 mL) and cooled to 0 °C. PMBCl (1.06 mL, 7.81 mmol) and TBAI (125 mg) were added before the addition of NaH (60% dispersion, 221 mg, 5.52 mmol). The resulting mixture was allowed to reach room temperature and was stirred overnight. Upon completion, the mixture was cooled to 0 °C and H_2O (100 mL) was slowly added to quench the reaction. The aqueous layer was extracted with EtOAc (3 x 75 mL) and the combined organics washed with H_2O (100 mL) and brine (100 mL). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by column chromatography (0 → 15% EtOAc in hexanes) yielding PMB-ether **9** (3,98 g, 78%) as a clear oil. ^1H NMR (300 MHz, $CDCl_3$): δ 3.55 – 3.61 (m, 2 H, H-5 and Ha-6) 3.73 (dd, J = 9.4 and 2.8 Hz, 1 H, H-3) 3.81 (s, 3 H, OCH_3) 3.95 – 4.02 (m, 2 H, H-4 and Hb-6) 4.14 (dd, J = 9.3 and 5.5 Hz, 1 H, H-2) 4.37 (d, J = 11.5 Hz, 1 H, $\underline{CH_2}$PhOMe) 4.45 (d, J = 11.5 Hz, 1 H, $\underline{CH_2}$PhOMe) 4.57 – 4.92 (m, 9 H, H-1, $\underline{CH_2}$Ph, CH=C=$\underline{CH_2}$) 5.43 (td, J = 6.6 and 5.3 Hz, 1 H, $\underline{CH}$=C=CH_2) 6.83 – 6.86 (m, 2 H, $CH_2\underline{Ph}$OMe) 7.18 – 7.24 (m, 2 H, $CH_2\underline{Ph}$OMe) 7.25 – 7.37 (m, 15 H, $CH_2\underline{Ph}$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.25, 68.10, 71.76, 72.85, 72.99, 73.09, 74.35, 74.86, 76.53, 76.70, 77.21, 78.92, 86.07, 113.74, 127.41, 127.46, 127.53, 127.56, 127.67, 128.14,

128.20, 128.28, 128.31, 129.45, 130.19, 138.44, 138.62, 138.67, 159.20, 208.91; Exact mass (ESI-MS) for $C_{38}H_{41}O_6$ $[M+H]^+$ found, 593.2900; calcd, 593.2898.

1-hydroxymethyl-6-*O*-p-methoxybenzyl-2,3,4-tri-*O*-benzyl-α-D-galactopyranose (10)

Ozone was bubbled through a solution of allene **9** (1.75 g, 3 mmol) in anhydrous DCM (80 mL) and MeOH (20 mL) at -78°C for 1h15 min. After flushing with oxygen, $NaBH_4$ (560 mg, 14.8 mmol) was added at 0°C and the reaction mixture was stirred for 2h. Water was added and the aqueous phase was extracted with DCM (3 x 50 ml). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (35% → 40% EtOAc in hexanes) to afford **10** (1.26 g, 73%) as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.07 (d, J = 5.7 Hz, 1 H, OH) 3.61 (dd, J = 10.5 and 4.5 Hz, 1 H, Ha-$\underline{CH_2}$OH) 3.65 – 3.73 (m, 1 H, Ha-6) 3.76 (dd, J = 6.8 and 2.7 Hz, 1 H, H-4) 3.80 – 3.82 (m, 4 H, Hb-$\underline{CH_2}$OH and OCH_3) 3.81 – 3.85 (m, 1 H, Hb-6) 3.85 – 3.92 (m, 1 H, H-5) 4.01 (dd, J = 3.6 and 2.9 Hz, 1 H, H-3) 4.04 – 4.12 (m, 2 H, H-1 and H-2) 4.39 – 4.75 (m, 8 H, $\underline{CH_2}$Ph and $\underline{CH_2}$PhOMe) 6.84 – 6.89 (m, 2 H, $CH_2\underline{Ph}$OMe) 7.21 – 7.28 (m, 2 H, $CH_2\underline{Ph}$OMe) 7.28 – 7.38 (m, 15 H, $CH_2\underline{Ph}$); ^{13} C NMR (75 MHz, $CDCl_3$): δ 55.25, 60.64, 67.10, 71.44, 72.97, 73.04, 73.13, 73.28, 74.03, 76.02, 104.74, 113.79, 127.50, 127.65, 127.70, 127.89, 127.97, 128.00, 128.32, 128.38, 128.48, 129.42, 129.49, 129.69, 130.13, 137.78, 138.26, 138.31, 159.22; Exact mass (ESI-MS) for $C_{36}H_{40}KO_7$ $[M+K]^+$ found, 623.2403; calcd, 623.2406.

(3S,4S,5R)-1-(2',3',4'-tri-O-benzyl-6'-O-p-methoxybenzyl-α-*C*-D-galactopyranosyl)-3-tert-butyloxycarbonylamino-4,5-Di-*O*-isopropylidene-1-nonadecene-4,5-diol (12)

To a solution of alcohol **10** (538 mg, 0.92 mmol) in DCM (20 ml) was added Dess-Martin periodinane (468 mg, 1.1 mmol) and the reaction mixture was stirred at room temperature for 2h. Upon disappearance of the starting material as judged by TLC, saturated $NaHCO_3$ solution (10 mL) was added to quench the reaction. The aqueous layer was extracted with DCM (3 x10 ml) and the combined organic phases were dried over Na_2SO_4, filtered and concentrated to afford the crude aldehyde which was used without further purification in the next step.

Lithium bis(trimethylsilyl)amide (1 M in THF, 1.84 mL, 1.84 mmol) was slowly added to a solution of sulfone **11** (538 mg, 0.92 mmol) in anhydrous THF (15 mL) at -78°C. After 1h, the above prepared crude aldehyde in THF (20 mL) was added dropwise over a period of 45 minutes. The mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with water (20 mL) and extracted with Et_2O (3x 20 mL). The combined organic phases were washed with water and brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (toluene/EtOAc: 95/5) to afford alkene **12** (428 mg, 46%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, J = 6.8 Hz, 3 H, terminal CH_3) 1.17 – 1.34 (m, 25 H, CH_3 and CH_2) 1.39 (s, 3 H, CH_3) 1.43 (s, 9 H, tBu) 1.48 – 1.71 (m, 4 H, CH_2) 3.51 – 3.67 (m, 3 H, H-4" and CH_2-6") 3.80 (s, 3 H, OCH_3) 3.93 – 4.10 (m, 4 H, H-4, H-2", H-3" and H-5") 4.10 – 4.20 (m, 1 H, H-5) 4.28 – 4.74 (m, 10 H, $\underline{CH_2}$Ph, $\underline{CH_2}$PhOMe, NH, H-3 and H-1") 4.79 – 4.95 (m, 1 H, $\underline{CH_2}$Ph) 5.90 (dd, J = 16.1 and 3.2 Hz, 1 H, H-1) 5.98 (dd, J = 16.4 and 4.0 Hz, 1 H, H-2) 6.82 – 6.89 (m, 2 H, $CH_2\underline{Ph}$OMe) 7.09 – 7.43 (m, 17 H, $CH_2\underline{Ph}$ and $CH_2\underline{Ph}$OMe); ^{13} C NMR (75 MHz, $CDCl_3$): δ 14.12, 22.69, 25.44, 26.86, 27.31, 28.18, 28.36, 28.96, 29.36, 29.58, 29.64, 29.66, 29.70, 31.92, 52.22, 55.23, 67.91, 71.65, 72.58, 72.90, 72.92, 73.24, 74.05, 74.96, 76.78, 77.21, 77.75, 79.47, 79.57, 107.98, 111.33, 113.70, 113.84, 122.63, 123.22, 123.95, 126.10, 126.43, 127.33, 127.42, 127.48, 127.53, 127.79, 128.04, 128.18, 128.25, 128.30, 128.57, 129.38, 129.71, 130.35, 131.38, 135.00, 138.54, 138.66, 138.69, 154.95, 159.13, 171.73; Exact mass (ESI-MS) for $C_{62}H_{87}NNaO_{10}$ $[M+Na]^+$ found, 1028.6207; calcd, 1028.6222.

(3S,4S,5R)-1-(2',3',4'-tri-O-benzyl-6'-hydroxy-α-*C*-D-galacto-pyranosyl)-3-tert-butyloxycarbonylamino-4,5-Di-*O*-isopro-pylidene-1-nonadecene-4,5-diol (13)

To a solution of PMB-ether **12** (428 mg, 0.43 mmol) in acetonitrile (14 ml) and H_2O (2 ml) was added CAN (581 mg, 1.06 mmol) at 0°C. The mixture was stirred for 50 minutes at 0 °C and was quenched with saturated $NaHCO_3$ solution (10 ml). The aqueous layer was extracted with EtOAc (3 x 10 ml) and the combined organic phases washed with saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered through a patch of celite and concentrated. The residue was purified by flash chromatography (hexane/EtOAc: 85/15) to afford alcohol **13** (197 mg, 73% based on starting material recovery), recovered starting material (123 mg) and acetonide cleaved product (20 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, J = 6.6 Hz, 3 H, terminal CH_3) 1.20 – 1.36 (m, 25 H, CH_3 and CH_2) 1.40 (s, 3 H, CH_3) 1.44 (s, 9 H, tBu) 1.48 – 1.77 (m, 4 H, CH_2) 1.95 (d, J = 6.8 Hz, 1 H, OH) 3.53 – 3.65 (m, 1 H, Ha-6") 3.64 (dd, J = 8.2 and 2.8 Hz, 1 H, H-3") 3.82 – 4.05 (m, 5 H, H-4, H-2", H-4", H-5" and Hb-6") 4.10 – 4.20 (m, 1 H, H-5) 4.27 – 4.37 (m, 1 H, H-3) 4.58 – 4.75 (m, 7 H, $\underline{CH_2}$Ph, NH and H-1") 4.49 (d, J = 11.6 Hz, 1 H, $\underline{CH_2}$Ph) 5.87 (dd, J = 16.1 and 3.3 Hz, 1 H, H-1) 5.96 (dd, J = 16.5 and 4.2 Hz, 1 H, H-2) 7.21 – 7.39 (m, 15 H, $CH_2\underline{Ph}$); ^{13} C NMR (75 MHz, $CDCl_3$): δ 14.11, 22.67, 25.39, 26.85, 27.20, 28.36, 28.82, 29.35, 29.54, 29.61, 29.64, 29.66, 29.68, 31.91, 52.18, 61.84, 72.10, 73.00, 73.29, 73.33, 73.56, 74.71, 76.86, 77.21, 77.71, 78.49, 79.51, 79.57, 108.02, 125.39, 126.20, 127.48, 127.55, 127.62, 127.66, 127.76, 127.86, 127.88, 127.94, 127.99, 128.06, 128.18, 128.25, 128.31, 128.39, 128.43, 128.51, 128.60, 128.67,

129.74, 129.81, 129.98, 131.50, 133.26, 137.46, 137.86, 138.12, 138.33, 138.42, 154.86, 154.90, 165.78; Exact mass (ESI-MS) for $C_{54}H_{83}N_2O_9$ $[M+NH_4]^+$ found, 903.6096; calcd, 903.6093.

(3S,4S,5R)-1-(6'-azido-2',3',4'-tri-O-benzyl-α-*C*-D-galacto-pyranosyl)-3-tert-butyloxycarbonylamino-4,5-Di-*O*-isopro-pylidene-1-nonadecene-4,5-diol (14)

To a solution of alcohol **13** (197 mg, 0.22 mmol) in anhydrous THF (15 ml) were added PPh_3 (231 mg, 0.88 mmol), DEAD (153 mg, 0.88 mmol), and DPPA (242 mg, 0.88 mmol) at -20°C. The mixture was allowed to warm to room temperature and stirred overnight. The solvent was evaporated under reduced pressure, and the residue was purified by flash chromatography (hexane/EtOAc: 9/1) to afford azide **14** (133 mg, 66%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, J = 6.6 Hz, 3 H, terminal CH_3) 1.20 – 1.36 (m, 25 H, CH_3 and CH_2) 1.40 (s, 3 H, CH_3) 1.44 (s, 9 H, tBu) 1.48 – 1.77 (m, 4 H, CH_2) 3.12 (dd, J = 12.9 and 4.3 Hz,1 H, Ha-6") 3.63 (dd, J = 8.0 and 2.6 Hz, 1 H, H-4") 3.73 (dd, J = 12.9 and 8.6 Hz, 1 H, Hb-6") 3.86 (t, J = 2.9 Hz, 1 H, H-3") 3.91 – 4.07 (m, 3 H, H-4, H-2", H-5") 4.11 – 4.27 (m, 1 H, H-5) 4.27 – 4.40 (m, 1 H, H-3) 4.53 – 4.74 (m, 7 H, $\underline{CH_2}$Ph, NH and H-1") 4.83 (d, J = 11.6 Hz, 1 H, $\underline{CH_2}$Ph) 5.86 (dd, J = 16.2 and 3.8 Hz, 1 H, H-1) 5.99 (dd, J = 16.5 and 4.2 Hz, 1 H, H-2) 7.23 – 7.42 (m, 15 H, $CH_2\underline{Ph}$); ^{13} C NMR (75 MHz, $CDCl_3$): δ 14.12, 22.69, 25.41, 26.91, 27.23, 28.36, 28.95, 29.36, 29.40, 29.46, 29.55, 29.62, 29.65, 29.67, 29.69, 31.92, 50.33, 52.21, 71.63, 72.23, 73.30, 73.35, 73.56, 74.60, 77.21, 77.73, 78.17, 79.48, 79.61, 108.03, 120.04, 120.08, 120.11, 120.15, 120.18, 120.25, 125.71, 127.49, 127.66, 127.71, 127.84, 127.88, 128.15, 128.34, 128.38, 128.41, 129.73, 129.83, 129.84, 130.04, 130.05, 131.72, 138.09, 138.26, 138.39, 154.96; Exact mass (ESI-MS) for $C_{54}H_{78}N_4NaO_8$ $[M+Na]^+$ found, 933.5705; calcd, 933.5712.

(3S,4S,5R)-1-(6'-azido-2',3',4'-tri-*O*-benzyl-α-*C*-D-galacto-pyranosyl)-3-hexacosylamino-1-nonadecene-4,5-diol (15)

To a solution of azide **14** (75 mg, 0.08 mmol) in DCM (4.5 mL) was added TFA (0.5 mL) and triethylsilane (0.25 mL). The resulting mixture was stirred 5h at room temperature and upon complete consumption of the starting material the solvents were evaporated under reduced pressure. The crude amine thus obtained was used without further purification in the next step. The amine was suspended in THF (5 mL) and a catalytic amount of 4-DMAP was added. Next p-nitrophenyl hexacosanoate (63 mg, 0.12 mmol) was added followed by addition of pyridine (5 mL). The resulting mixture was stirred for 3 days at room temperature. Evaporation of the solvents and purification of the resulting residue by means of column chromatography (hexane/EtOAc: 7/3) yielded **15** (55 mg, 60%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, J = 6.5 Hz, 6 H, 2 x terminal CH_3) 1.16 – 1.38 (m, 67 H, CH_2) 1.38 – 1.79 (m, 6 H, CH_2) 2.19 (t, J = 7.2 Hz, 2 H, CH_2) 3.87 (d, J = 6.6 Hz, 1 H, OH) 3.10 (dd, J = 13.5 and 3.2 Hz, 1 H, Hb-6") 3.47 – 3.59 (m, 2 H, H-4, H-2", H-5 and H-3") 3.66 (dd, J = 6.7 and 2.7 Hz, 1 H, H-4) 3.79 – 3.94 (m, 3 H, H-3, H-4" and Hb-6") 4.03 – 4.11 (m, 1 H, H-5") 4.47 – 4.77 (m, 8 H, $\underline{CH_2}$Ph, NH and H-1") 5.84 (dd, J = 15.9 and 4.0 Hz, 1 H, H-1) 5.92 – 6.02 (m, 2 H, H-2 and NH(CO)) 7.23 – 7.39 (m, 15 H, $CH_2\underline{Ph}$); ^{13} C NMR (75 MHz, $CDCl_3$): δ 14.12, 22.69, 25.75, 29.32, 29.36, 29.51, 29.60, 29.63, 29.66, 29.70, 31.92, 33.77, 36.88, 49.34, 53.51, 70.05, 72.86, 73.12, 73.25, 73.32, 73.85, 76.30, 76.76, 77.20, 115.63, 126.13, 127.60, 127.80, 127.91, 127.97, 128.25, 128.45, 129.28, 137.88, 137.91, 138.13, 141.08, 162.44, 173.30; Exact mass (ESI-MS) for $C_{77}H_{122}N_5O_7$ $[M+pyridine+H]^+$ found, 1228.9360; calcd, 1228.9339.

(3S,4S,5R)-1-(2',3',4'-tri-*O*-benzyl-6'-naphtureido-6'-deoxy-α-*C*-D-galactopyranosyl)-3-hexacosylamino-1-nonadecene-4,5-diol (16)

To a solution of azide **15** (89 mg, 0.08 mmol) in THF (3 mL) at room temperature, a 1 M solution of PMe_3 in THF (2.31 ml, 2.31 mmol) was added dropwise. After stirring for 4h at room temperature, H_2O (0.5 mL) was added and the reaction mixture was allowed to stir overnight at room temperature. Then the solvent was removed under reduced pressure. The crude product was dried by making azeotropic mixture with toluene to afford the crude amine. The crude amine was dissolved in anhydrous DMF (3 mL) and cooled to 0 °C. Next 1-naphthyl isocyanate (11 µL, 0.08 mmol) was added, the mixture was allowed to reach room temperature and was stirred overnight. Upon completion, the solvent was removed under reduced pressure and the residue purified by column chromatography (hexan/EtOAc: 5/5) to afford urea **16** (100 mg, quantitative yield) as a waxy solid. ^{1}H NMR (300 MHz, pyridine-d_5): δ 0.88 (t, J = 6.5 Hz, 6 H, 2 x terminal CH_3) 1.16 – 1.44 (m, 66 H, CH_2) 1.60 – 1.77 (m, 1 H, CH_2) 1.77 – 1.98 (m, 4 H, CH_2) 2.20 – 2.34 (m, 1 H, CH_2) 2.46 (t, J = 8.2 Hz, 2 H, CH_2) 3.91 – 4.03 (m, 2 H, H-4" and Ha-6") 4.06 – 4.18 (m, 2 H, H-3" and Hb-6") 4.20 – 4.29 (m, 2 H, H-4 and H-5) 4.36 (dd, J = 8.2 and 5.5 Hz, 1 H, H-5") 4.48 – 4.56 (m, 1 H, H-2") 4.68 – 4.84 (m, 5 H, $\underline{CH_2}$Ph) 4.90 – 5.06 (m, 3 H, H-1", $\underline{CH_2}$Ph and OH) 5.86 (t, J = 7.5 Hz, 1 H, H-3) 6.21 (br. s, 1 H, OH) 6.51 (br. s, 1 H, NH) 6.63 (dd, J = 15.7 and 4.1 Hz, 1 H, H-1) 6.85 (dd, J = 15.7 and 6.4 Hz, 1 H, H-2) 7.17 – 7.60 (m, 18 H, naphthyl and$CH_2\underline{Ph}$) 7.63 – 7.70 (m, 1 H, naphthyl) 7.87 – 7.94 (m, 1 H, naphthyl) 8.27 – 8.33 (m, 1 H, naphthyl) 8.48 – 8.56 (m, 2 H, naphthyl and NH(CO)) 9.36 (s, 1 H, NH); ^{13} C NMR (75 MHz, pyridine-d_5): δ 14.71, 23.36, 26.74, 26.91, 30.03, 30.05, 30.24, 30.30, 30.34, 30.36, 30.44, 30.47, 30.57, 30.81, 32.54, 32.56, 35.06, 37.37, 41.65, 54.17, 72.82, 73.14, 73.53, 73.65, 73.80, 74.84, 77.04, 77.95, 78.46, 119.98, 122.80, 123.20, 124.57, 124.80, 126.28, 126.50, 126.99, 127.41, 128.19, 128.24, 128.27, 128.54, 128.81, 129.03, 129.05, 129.17, 129.28, 132.68, 135.27, 136.53,

139.80, 139.85, 139.99, 149.41, 151.01, 157.85, 172.97; Exact mass (ESI-MS) for $C_{83}H_{126}N_3O_8$ $[M+H]^+$ found, 1292.9557; calcd, 1292.9539.

1-allyl-2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose (17)

To a solution of galactose pentaacetate (9 g, 23.06 mmol) in anhydrous acetonitrile (90 mL) at 0 °C, was added allylTMS (7.35 mL, 46.12 mmol) followed by dropwise addition of TMSOTf (4.17 mL, 46.12 mmol). The reaction mixture was stirred overnight at 0 °C. Upon disappearance of the starting material the mixture was quenched by slow addition of a saturated $NaHCO_3$ solution. The aqueous layer was extracted with DCM (3 x 100 mL) and the combined organic layers washed with H_2O (150 mL) and brine (150 mL). The organics were dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting residue was subjected to column chromatography (hexanes/EtOAc : 7/3) furnishing a mixture of both α and β anomers in a 7:1 ratio.

To a solution of the α:β mixture (5.52 g, 14.8 mmol) in methanol (55 mL) was added, sodium methoxide (5.4 M solution in MeOH) till pH 10. The reaction was stirred 4 hours at room temperature, next the reaction mixture was diluted with methanol and neutralized with amberlyte IR120 H^+-form. The resin was filtered off and the filtrate was concentrated under reduced pressure. The residue was crystallized from methanol/diethyl ether by dissolution in minimum boiling methanol with addition of ether until the cloud point, followed by slow cooling to -20 °C. Pure alpha anomer crystals were collected by filtration and were reacetylated by treatment with 15 mL of acetic anhydride and 15 mL of pyridine followed by stirring overnight at room temperature. The reaction was slowly poured into ice water (200 mL) and then extracted with EtOAc (3 x 200 mL). The organic layer was washed with saturated $NaHCO_3$ solution until the evolution of gasses ceased (2 x 200 mL), and then washed with H_2O (200 mL), and brine (200 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure yielding pure α-anomer **17** (3.83 g, 44% over 3 steps) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.03 (s, 3 H, CH_3) 2.04 (s, 3 H, CH_3) 2.07 (s, 3 H, CH_3) 2.12 (s, 3 H, CH_3) 2.23 – 2.34 (m, 1 H, CH=$\underline{CH_2}$a) 2.41 – 2.54 (m, 1 H, CH=$\underline{CH_2}$b) 4.05 – 4.13 (m, 2 H, CH_2-6) 4.16 – 4.23 (m, 1 H, H-2) 4.30 (ddd, J = 10.2, 5.2 and 4.8 Hz, 1H, H-1) 5.08 – 5.17 (m, 2 H, $\underline{CH_2}$CH=CH_2) 5.21 (dd, J = 9.3 and 3.2 Hz, 1 H, H-5) 5.28 (dd, J = 9.3 and 4.8 Hz, 1 H, H-4) 5.40 – 5.44 (m, 1 H, $\underline{H\text{-}3}$) 5.68 – 5.83 (m, 1 H, $\underline{CH}$=CH_2); ^{13} C NMR (75 MHz, $CDCl_3$): δ 20.71, 20.77, 20.83, 30.93, 61.52, 67.65, 67.93, 68.25, 68.27, 71.47, 117.69, 133.42, 169.85, 169.96, 170.13, 170.57; Exact mass (ESI-MS) for $C_{17}H_{25}O_9$ $[M+H]^+$ found, 373.1498; calcd, 373.1493.

1-propenyl-2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose (18)

To a solution of allylsugar **17** (6.96 g, 18.69 mmol) in toluene (1 L) was added bis(benzonitrile) palladium(II) chloride (717 mg, 1.87 mmol) and the mixture was heated to 90 °C and stirred for 3 days. The reaction was monitored by NMR and upon completion the reaction mixture was filtered through a patch of celite and evaporated under reduced pressure. The residue was purified by flash column chromatography (0 → 30 % EtOAc in hexanes) to afford a mixture of E and Z-alkene sugars **18** (4.38 g, 63%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.78 (dt, J = 6.4 and 1.5 Hz, 3H, terminal CH_3) 2.01 (s, 3 H, CH_3) 2.04 (s, 3 H, CH_3) 2.04 (s, 3 H, CH_3) 2.14 (s, 3 H, CH_3) 4.03 – 4.19 (m, 3 H, CH_2-6 and H-5) 4.74 (tt, J = 5.9 and 1.5 Hz, 1 H, H-1) 5.01 – 5.34 (m, 2 H, H-3 and H-2) 5.41 (dd, J = 4.8 and 3.2 Hz, 1 H, H-4) 5.56 – 5.70 (m, 1 H, CH=$\underline{CH}$$CH_3$) 5.82 – 5.98 (m, 1 H, $\underline{CH}$=$CHCH_3$); ^{13} C NMR (75 MHz, $CDCl_3$): δ 18.31, 20.67, 20.70, 20.78, 61.82, 68.02, 68.08, 68.33, 73.15, 122.58, 133.20, 169.94, 170.09, 170.22, 170.54; Exact mass (ESI-MS) for $C_{17}H_{25}O_9$ $[M+H]^+$ found, 373.1496; calcd, 373.1493.

1-propenyl-α-D-galactopyranose (19)

To a solution of **18** (1.72 g, 4.62 mmol) in methanol (30 mL) was added sodium methoxide (5.4M NaOMe in MeOH) till pH 10. The reaction was allowed to stir overnight at room temperature. Subsequently, the mixture was neutralized with Amberlite IR 120 (H^+ form) and diluted with methanol. After filtration and rinsing with methanol, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (0 → 20% MeOH in DCM) affording sugar **19** (874 mg, 93%) as a white solid. ^{1}H NMR (300 MHz, $MeOD_3$): δ 1.74 – 1.78 (m, 3H, terminal CH_3) 3.58 (dd, J = 9.7 and 3.2 Hz, 1 H, H-3) 3.63 – 3.86 (m, 3H, H-5 and CH_2-6) 3.89 (dd, J = 3.2 and 1.7 Hz, 1 H, H-2) 3.94 (dd, J = 9.7 and 5.8 Hz, 1 H, H-4) 4.41 (tt, J = 5.7 and 1.2 Hz, 1 H, H-1) 5.73 – 5.94 (m, 2 H, CH=CH); ^{13} C NMR (75 MHz $MeOD_3$): δ 18.57, 62.57, 69.73, 70.67, 72.06, 73.56, 76.96, 125.44, 132.13; Exact mass (ESI-MS) for $C_9H_{17}O_5$ $[M+H]^+$ found, 205,1059; calcd, 205.1071.

1-propenyl-6-*O*-triisopropylsilyl-α-D-galactopyranose (20)

To a solution of **19** (2.14 g, 10.46 mmol) in anhydrous DMF (45 mL) at 0 °C was added imidazole (1.42 g, 20.92 mmol) and TIPSCl (2.9 mL, 13.60 mmol). The reaction mixture was allowed to reach room temperature and was stirred overnight. Upon completion of the reaction H_2O (100 mL) was added and the aqueous layer was extracted with Et_2O (3 x 75 mL). The combined organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The residue was purified by flash column chromatography (45 → 75% EtOAc in hexanes) affording silyl ether **20**

(3.19 g, 84%) as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.02 - 1.11 (m, 21 H, i-prop) 1.77 (dt, J = 6.4 and 1.5 Hz, 3 H, terminal CH_3) 2.36 – 2.37 (br. s, 3H, 3 x OH) 3.63 (dd, J = 9.7 and 3.4 Hz, 1 H, H-3) 3.75 – 4.00 (m, 3H, H-5 and CH_2-6) 4.06 (dd, J = 9.6 and 6.0 Hz, 1 H, H-2) 4.13 (dd, J = 3.4 and 1.6 Hz, 1 H, H-4) 4.53 (t, J = 6.0 Hz, 1 H, H-1) 5.67 - 5.77 (m, 1 H, CH=CHCH$_3$) 5.85 – 5.99 (m, 1 H, CH=CHCH$_3$); ^{13} C NMR (75 MHz, $CDCl_3$): δ 11.80, 17.88, 18.25, 63.66, 63.89, 69.34, 69.95, 70.08, 71.23, 71.32, 71.76, 75.78, 77.20, 123.56, 132.47; Exact mass (ESI-MS) for $C_{18}H_{37}O_5Si$ $[M+H]^+$ found, 361.2407; calcd, 361.2405.

2,3,4-tri-*O*-(4-methoxybenzyl)-1-propenyl-6-*O*-tri-isopropylsilyl-α-D-galactopyranose (21)

Sugar **20** (3.19 g, 8.83 mmol) was dissolved in anhydrous DMF (100 mL) and cooled to 0 °C. PMBCl (6.0 mL, 44.15 mmol) and TBAI (500 mg) were added before the addition of NaH (60% dispersion, 1.77 g, 44.15 mmol). The resulting mixture was heated to 40 °C and stirred overnight. Upon completion, the mixture was cooled to 0 °C and H_2O (300 mL) was slowly added to quench the reaction. The aqueous layer was extracted with EtOAc (3 x 200 mL) and the combined organics washed with H_2O (200 mL) and brine (200 mL). The organic layer was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc: 9/1) yielding alkene **21** (6.12 g, 96%) as a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.98 – 1.06 (m, 21 H, i-prop) 1.70 – 1.76 (m, 3 H, terminal CH_3) 3.47 – 3.74 (m, 4 H, H-3, H-5 and CH_2-6) 3.76 – 3.83 (m, 9 H, 3 x OCH_3) 3.88 – 3.92 (m, 1 H, H-4) 4.06 (dd, 1 H, J = 9.5 and 5.9 Hz, H-2) 4.36 – 4.85 (m, 7 H, H-1 and 3 x CH_2PhOMe) 5.65 – 5.91 (m, 2 H, CH=CH) 6.79 – 6.89 (m, 6 H, arom. H) 7.17 – 7.31 (m, 6H, arom. H); ^{13} C NMR (75 MHz, $CDCl_3$): δ 11.88, 12.52, 17.97, 18.08, 18.12, 18.18, 55.22, 55.25, 62.21, 67.95, 70.65, 71.92, 72.34, 72.50, 72.57, 72.65, 72.94, 73.12, 73.34, 73.63, 74.02, 74.22, 74.53, 74.76, 77.20, 79.49, 110.00, 113.54, 113.67, 113.73, 124.84, 125.91, 128.96, 128.99, 129.39, 129.45, 129.62, 129.68, 129.77, 129.92, 130.46, 130.82, 130.85, 131.11, 131.14, 159.02, 159.09; Exact mass (ESI-MS) for $C_{42}H_{60}NaO_8Si$ $[M+Na]^+$ found, 743.3948; calcd, 743.3950.

2,3,4-tri-*O*-(4-methoxybenzyl)-1-(1,2-di-hydroxypropyl)-6-*O*-triisopropylsilyl-α-D-galactopyranose (22)

To a solution of **21** (2 g, 2.77 mmol) in THF (8.5 mL) and H_2O (1.3 mL) was added NMO (976 mg, 8.33 mmol) and K_2OsO_4 (50 mg, 0.14 mmol). The reaction was allowed to stir overnight at room temperature and was then quenched with a saturated Na_2SO_3 solution (10 mL). After 30 minutes of stirring H_2O (50 mL) was added and the aqueous layer was extracted with EtOAc (3 x 40 mL). The combined organic layers were washed successively with 0.6 M HCl solution (40 mL), saturated $NaHCO_3$ solution (40 mL) and brine (40 mL). The organic phase was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash column chromatography (10 → 30% EtOAc in hexanes) yielding diol **22** (1.37 g, 65%) as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) (isomers): δ 0.92 – 1.11 (m, 21 H, i-prop) 1.16 – 1.24 (m, 3 H, terminal CH_3) 1.99 (br. s, 1 H, OH) 2.20 (br. s, 1 H, OH) 3.46 – 3.76 (m, 3 H, H-1', H-3 and Ha-6) 3.77 – 3.83 (m, 9 H, 3 x OCH_3) 3.83 – 4.03 (m, 3 H, H-2, H-4 and H-5) 4.03 – 4.25 (m, 2 H, H-1 and H-2') 4.27 – 4.40 (m, 1 H, Hb-6) 4.40 – 4.71 (m, 6 H, 3 x CH_2PhOMe) 6.81 – 6.90 (m, 6 H, arom. H) 7.12 – 7.26 (m, 6 H, arom. H); ^{13} C NMR (75 MHz, $CDCl_3$) (isomers): δ 11.94, 12.57, 17.94, 18.08, 55.28, 59.80, 65.31, 66.50, 66.91, 68.79, 69.14, 69.35, 71.44, 71.58, 71.83, 71.93, 72.39, 72.51, 72.56, 72.89, 73.17, 73.35, 75.00, 75.38, 113.68, 113.73, 113.77, 113.86, 114.31, 129.21, 129.34, 129.37, 129.59, 129.77, 129.94, 129.98, 130.23, 130.32, 130.46, 131.98, 159.20, 159.29, 159.46; Exact mass (ESI-MS) for $C_{42}H_{62}KO_{10}Si$ $[M+K]^+$ found, 793.3746; calcd, 793.3744.

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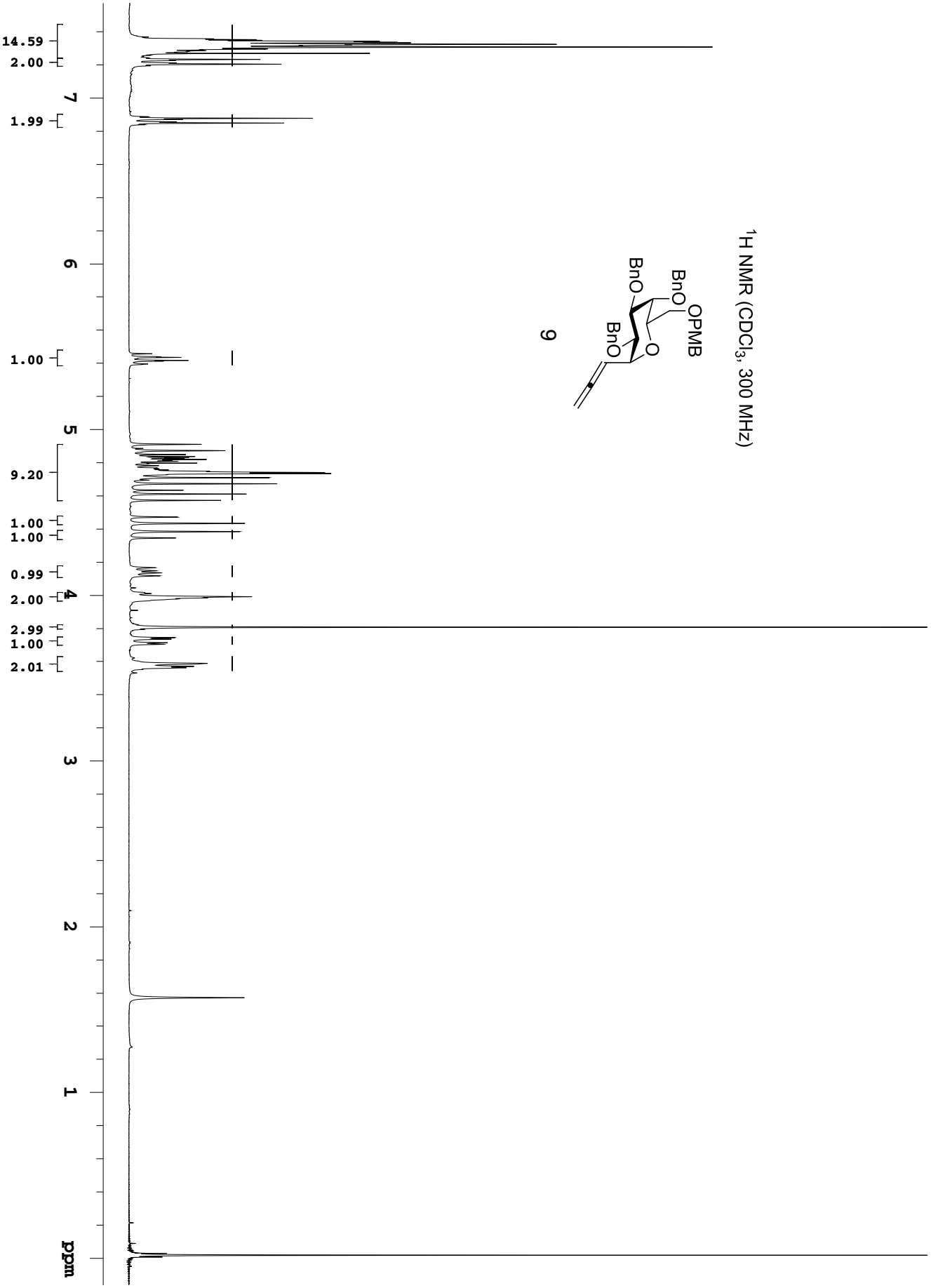
[1] S.-C., Hung; C.-C ., Lin; C.-H.,Wong, *Tetrahedron letters*, 1997, **31**, 5419.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1.00
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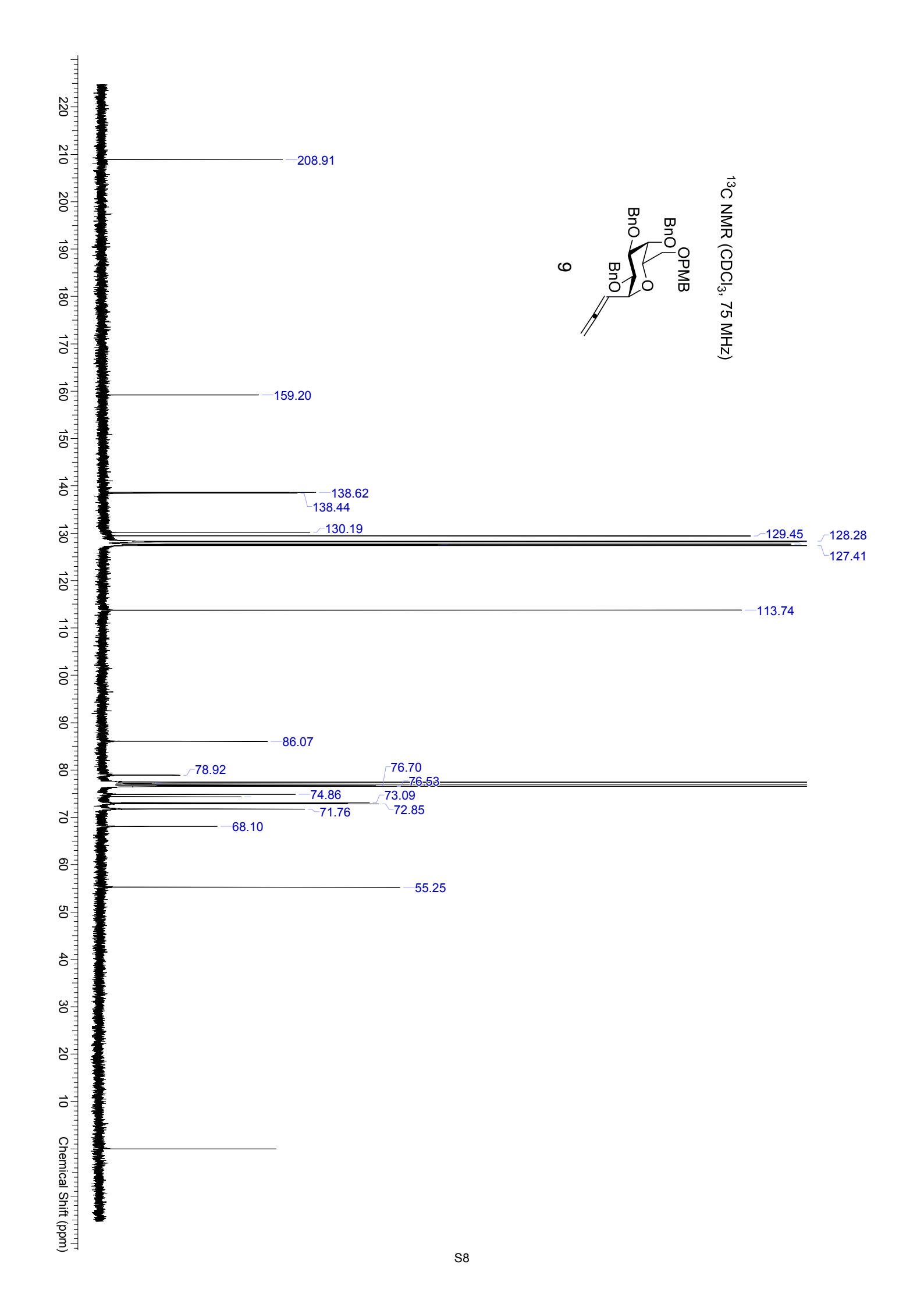
1.00
0.99
2.00
2.99
1.00
2.01
7
6
5
4
3
2
1
ppm
9
BnO
BnO
OPMB
O
BnO
^{1}H NMR (CDCl$_3$, 300 MHz)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BnO
OPMB
BnO
O
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128.28
127.41
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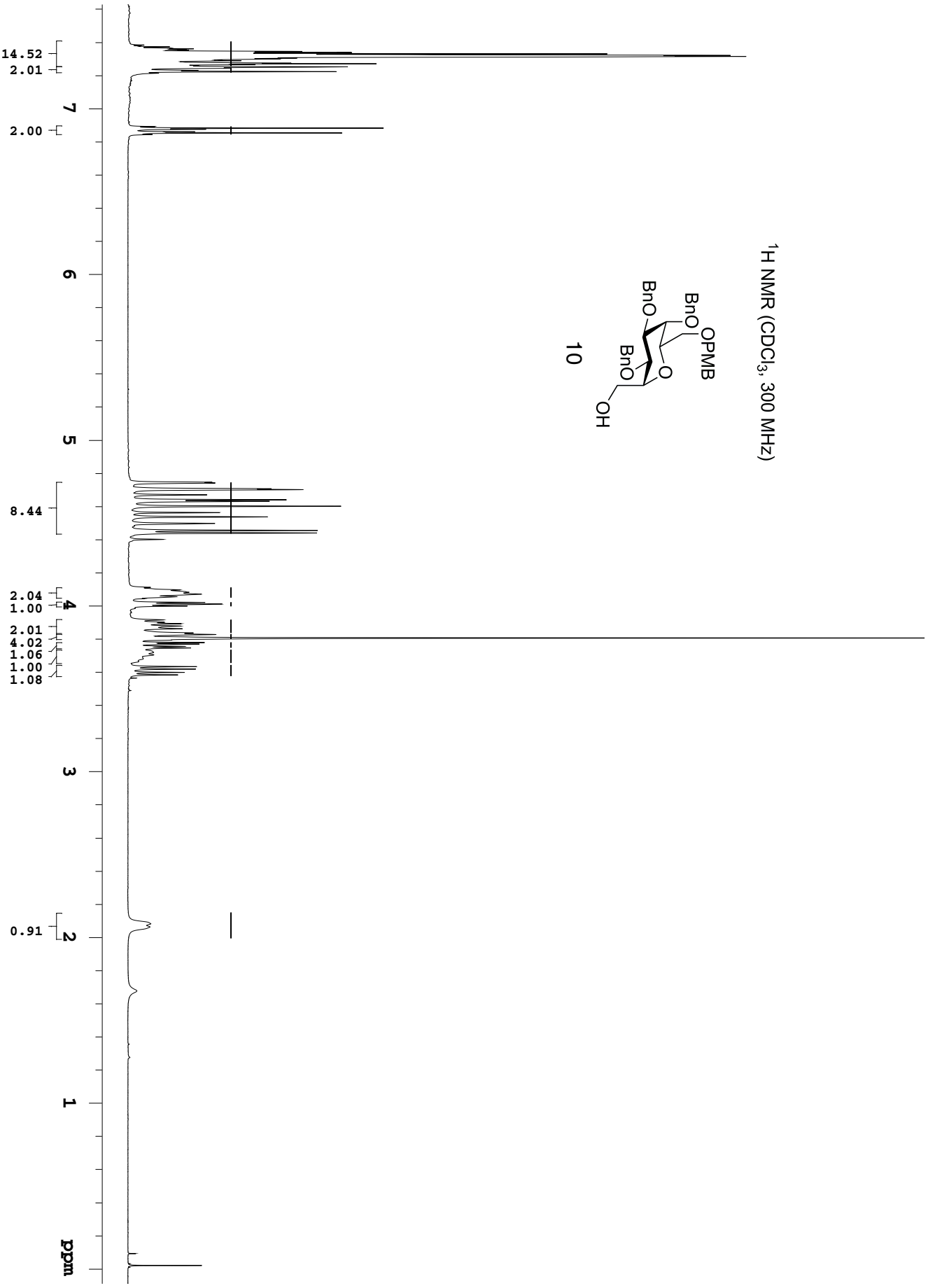
71.76
68.10
55.25
Chemical Shift (ppm)


^{1}H NMR (CDCl$_3$, 300 MHz)
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BnO
OPMB
O
BnO
OH
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2.00
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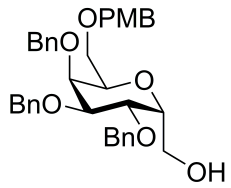
2.04
1.00
2.01
4.02
1.06
1.00
1.08
0.91
10
7
6
5
4
3
2
1
ppm

^{13}C NMR ($CDCl_3$, 75 MHz)



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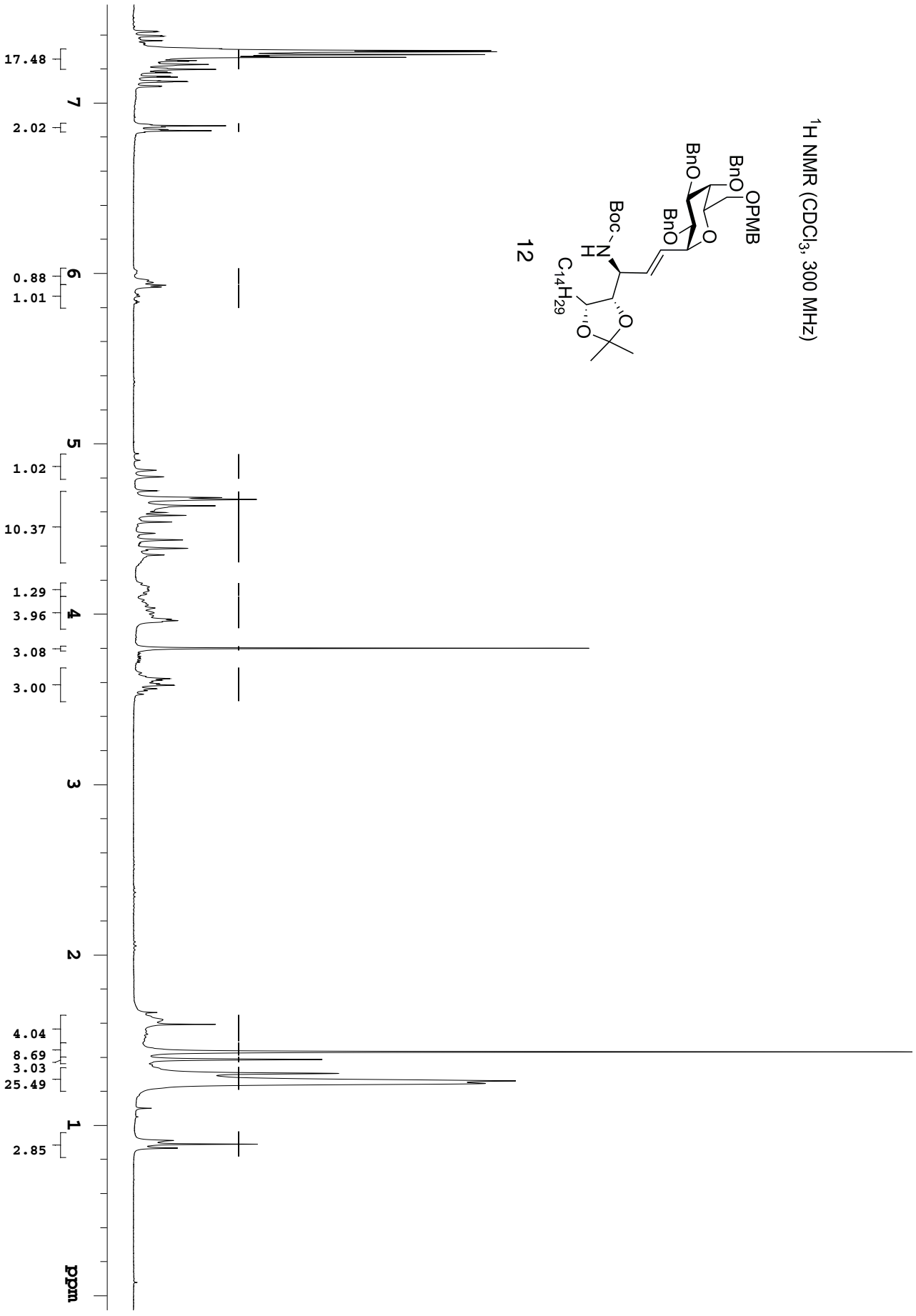
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2.02
0.88
1.01
1.02
10.37
1.29
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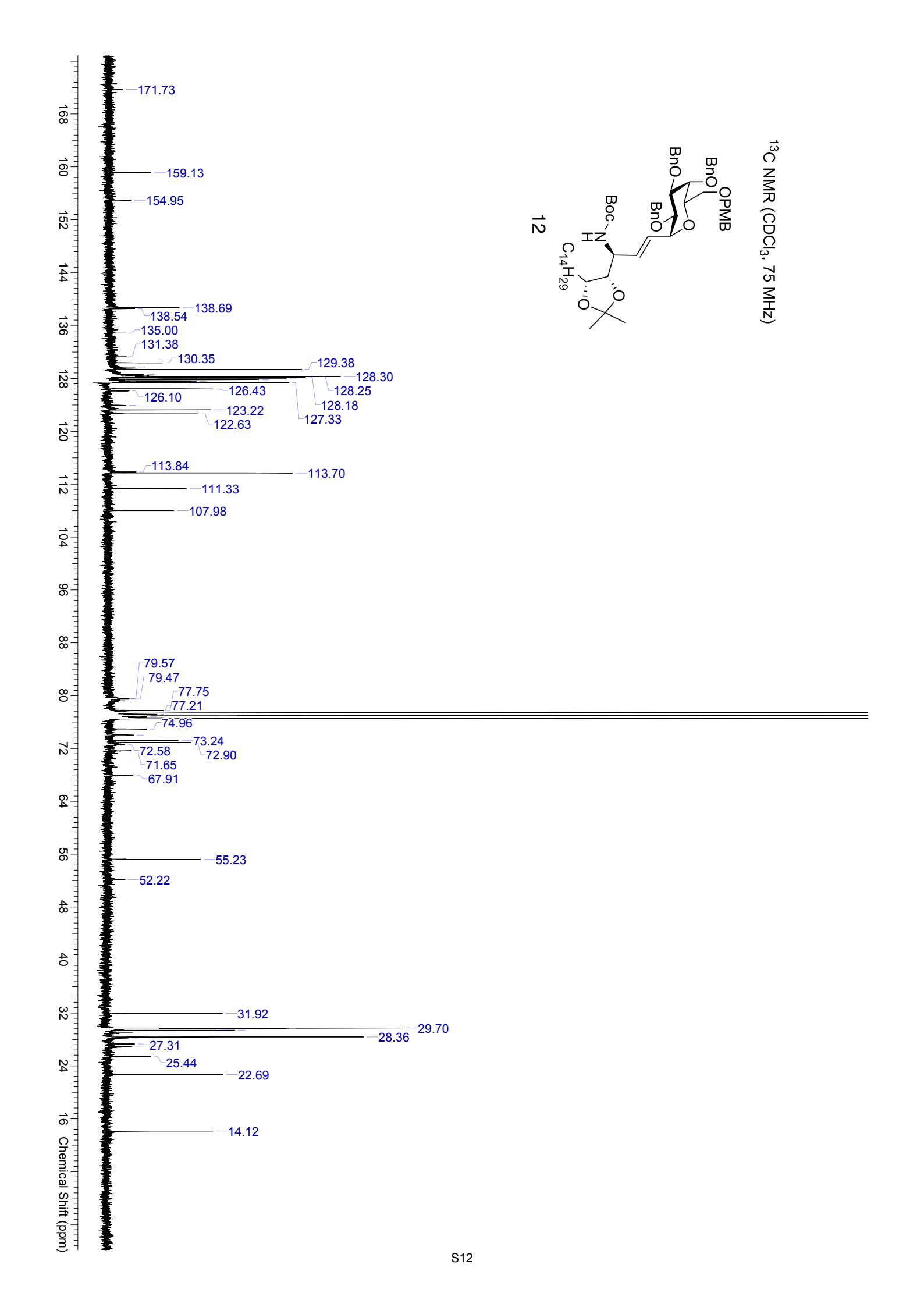
4.04
8.69
3.03
25.49
2.85
ppm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12
Boc
N
H
$C_{14}H_{29}$
BnO
BnO
BnO
OPMB
O
O
O
171.73
159.13
154.95
138.69
138.54
135.00
131.38
130.35
129.38
128.30
128.25
128.18
127.33
126.43
126.10
123.22
122.63
113.84
113.70
111.33
107.98
79.57
79.47
77.75
77.21
74.96
73.24
72.90
72.58
71.65
67.91
55.23
52.22
31.92
29.70
28.36
27.31
25.44
22.69
14.12
168
160
152
144
136
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120
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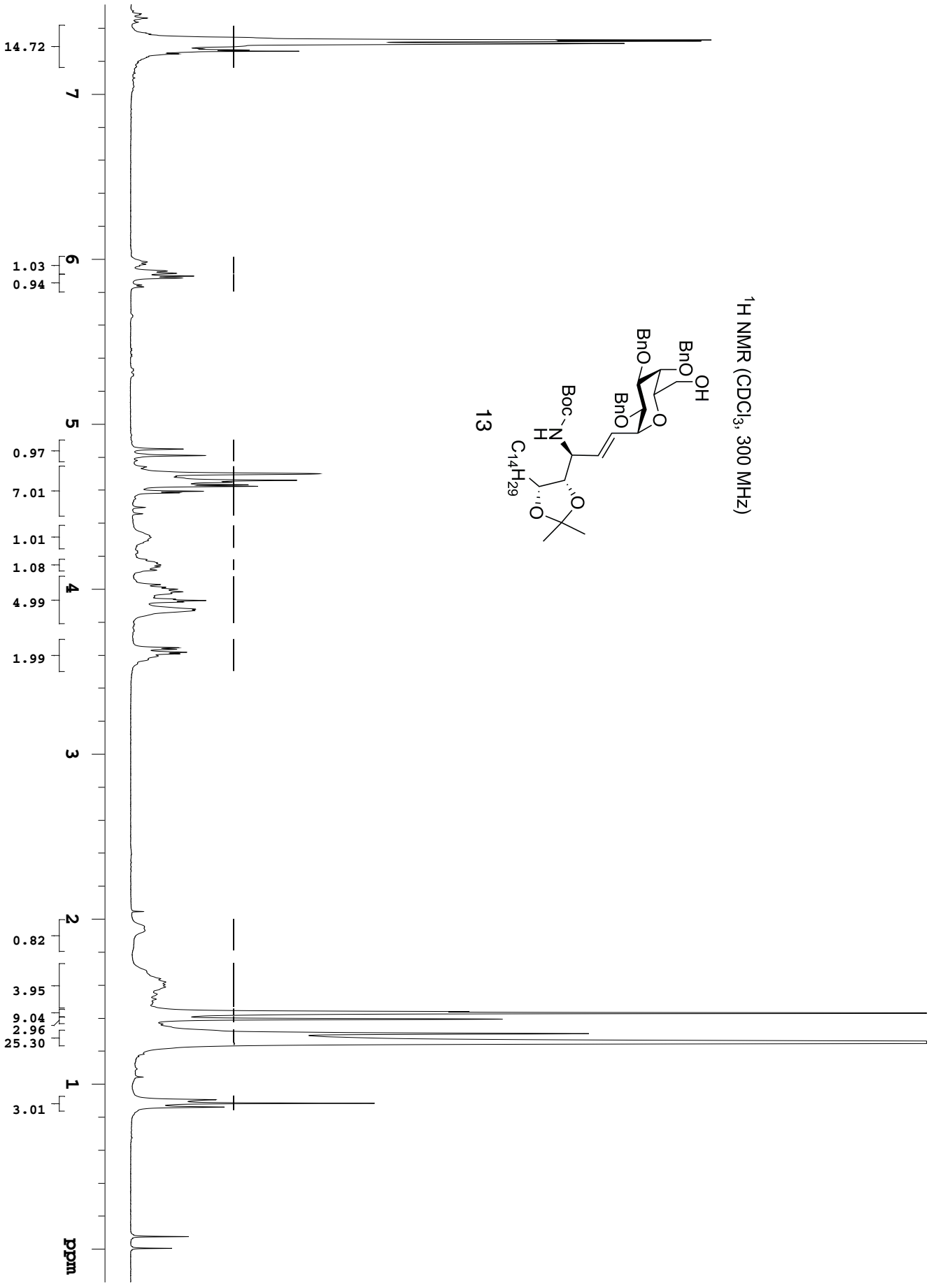
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)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1.08
4.99
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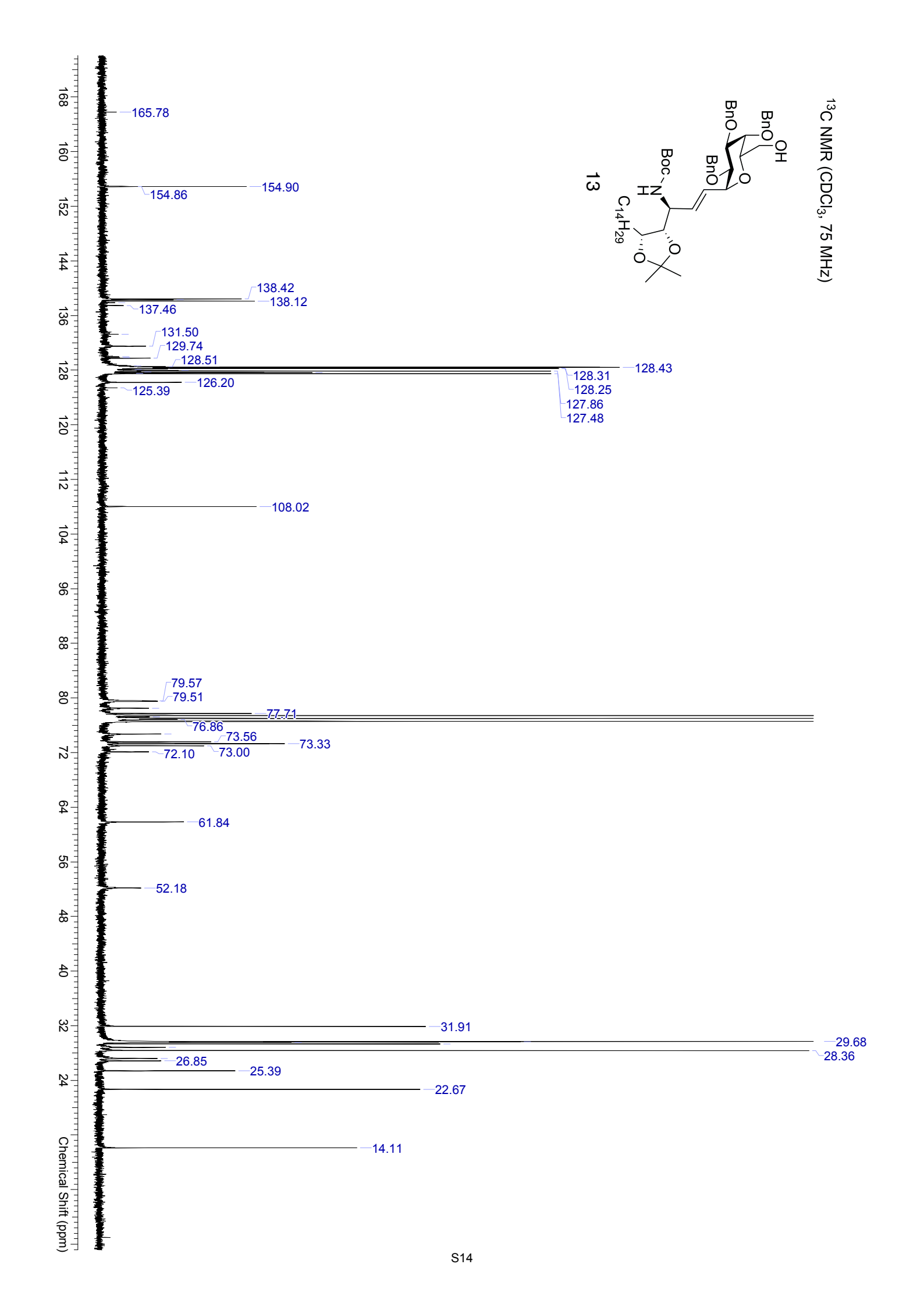
2.96
25.30
3.01
7
6
5
4
3
2
1
ppm
13
Boc
N
H
$C_{14}H_{29}$
BnO
BnO
BnO
OH
O
O
O
^{1}H NMR ($CDCl_3$, 300 MHz)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BnO
OH
BnO
O
Boc
N
H
$C_{14}H_{29}$
O
O
165.78
154.90
154.86
138.42
138.12
137.46
131.50
129.74
128.51
128.43
128.31
128.25
127.86
127.48
126.20
125.39
108.02
79.57
79.51
77.71
76.86
73.56
73.33
73.00
72.10
61.84
52.18
31.91
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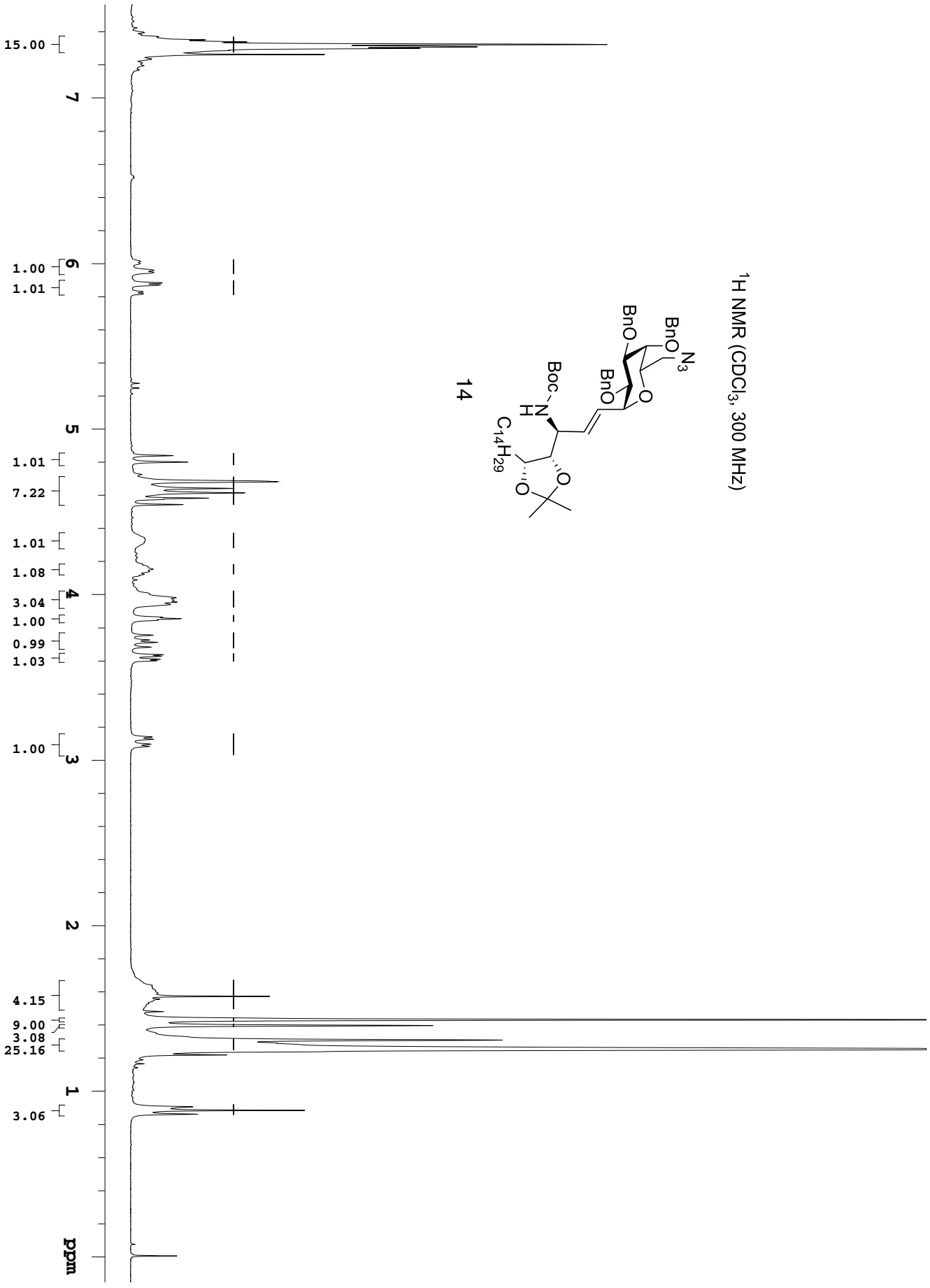
25.39
22.67
14.11
Chemical Shift (ppm)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1.08
3.04
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1.03
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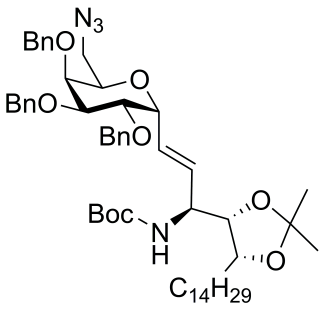
4.15
9.00
3.08
25.16
3.06
ppm
1
2
3
4
5
6
7
14
^{1}H NMR (CDCl$_3$, 300 MHz)

^{13}C NMR ($CDCl_3$, 75 MHz)



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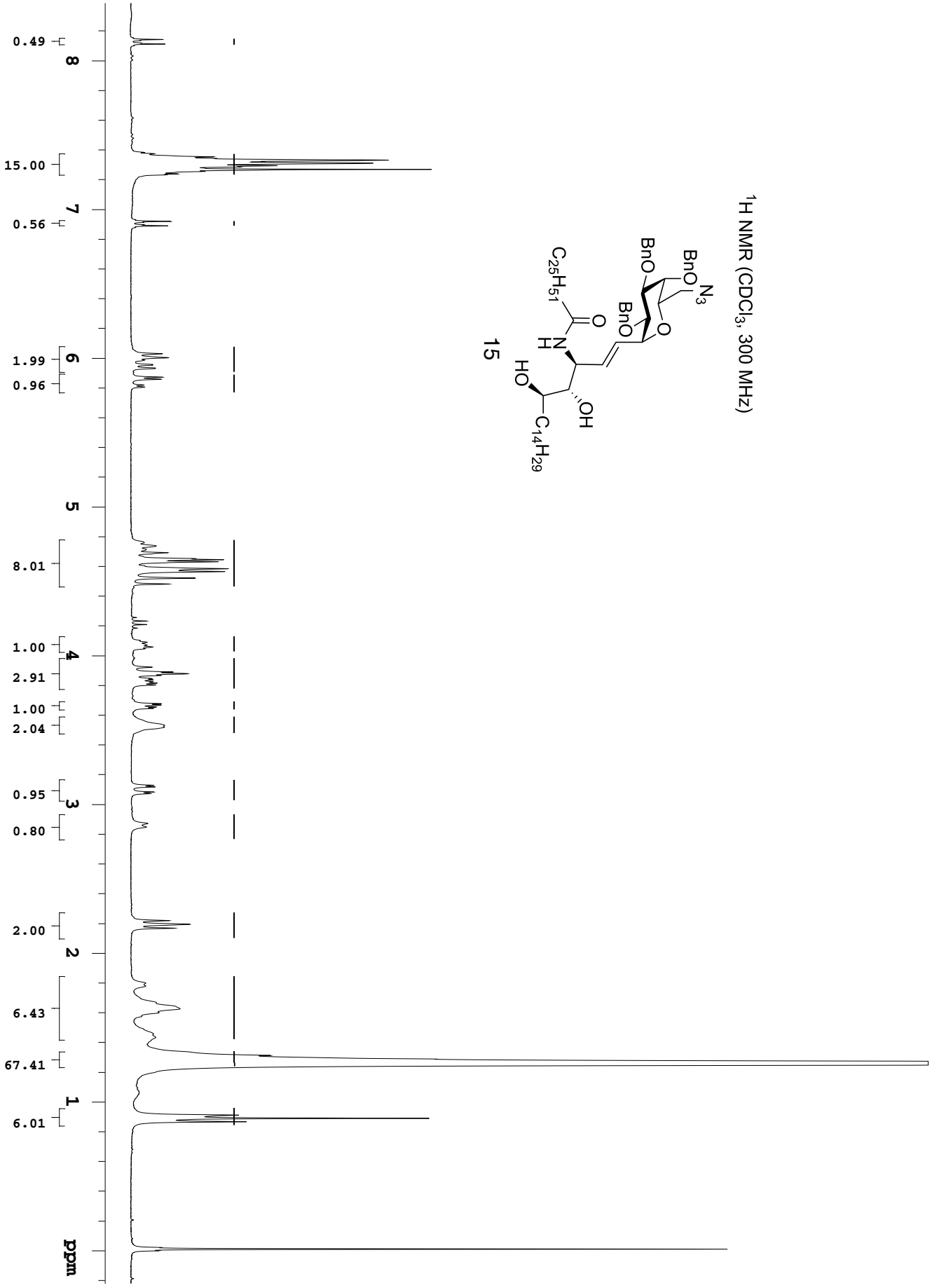
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1.00
2.91
1.00
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7
6
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4
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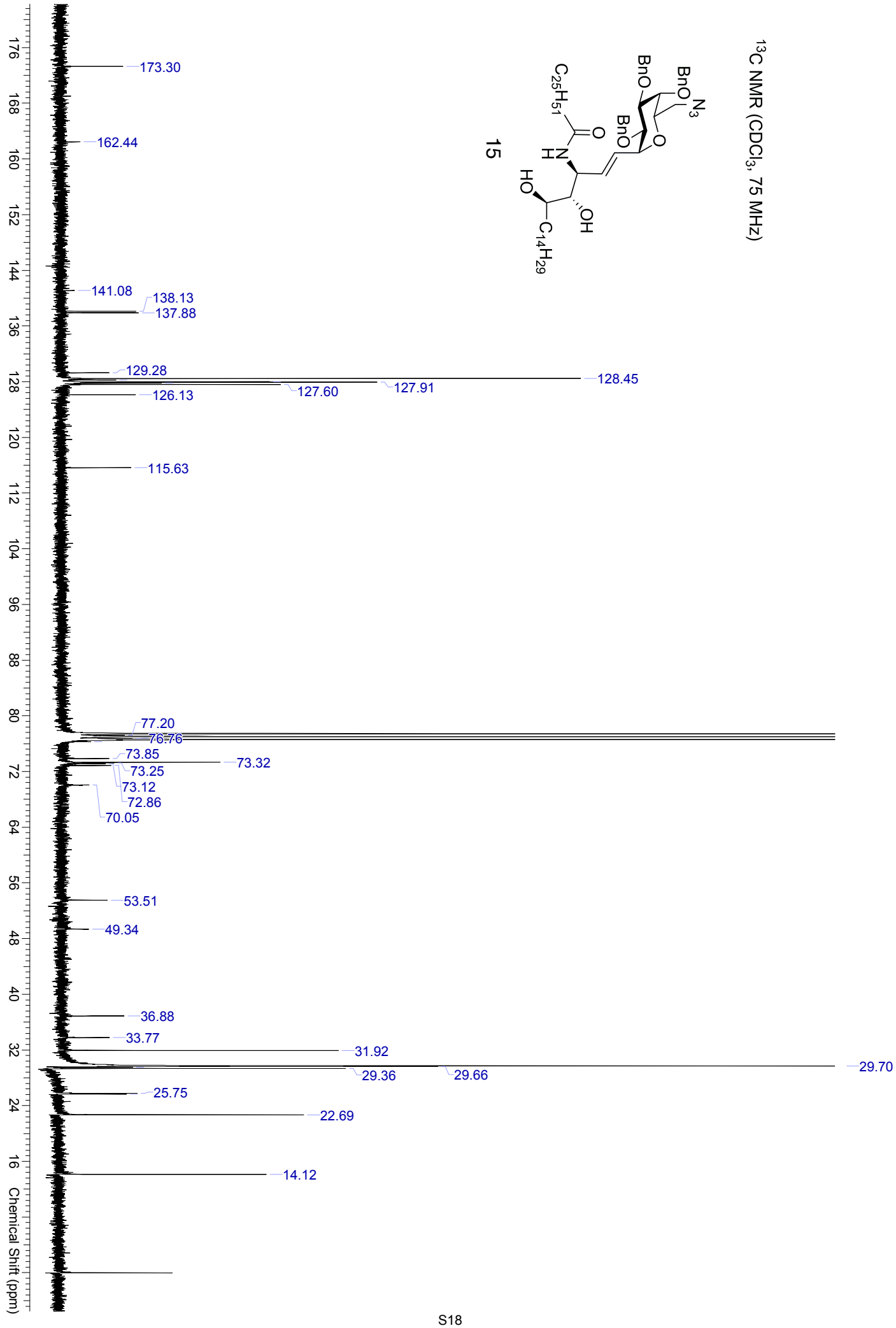
2
1
ppm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$C_{25}H_{51}$
$C_{14}H_{29}$
BnO
BnO
BnO
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O
N
H
HO
OH
173.30
162.44
141.08
138.13
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129.28
128.45
127.60
127.91
126.13
115.63
77.20
76.76
73.85
73.32
73.25
73.12
72.86
70.05
53.51
49.34
36.88
33.77
31.92
29.70
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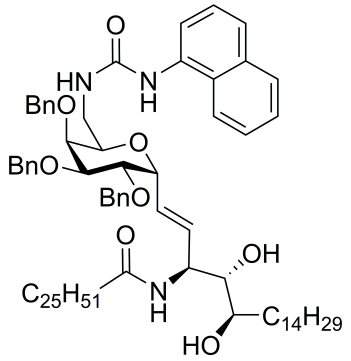
29.66
25.75
22.69
14.12
Chemical Shift (ppm)

^{1}H NMR (pyridine-d$_5$, 300 MHz)



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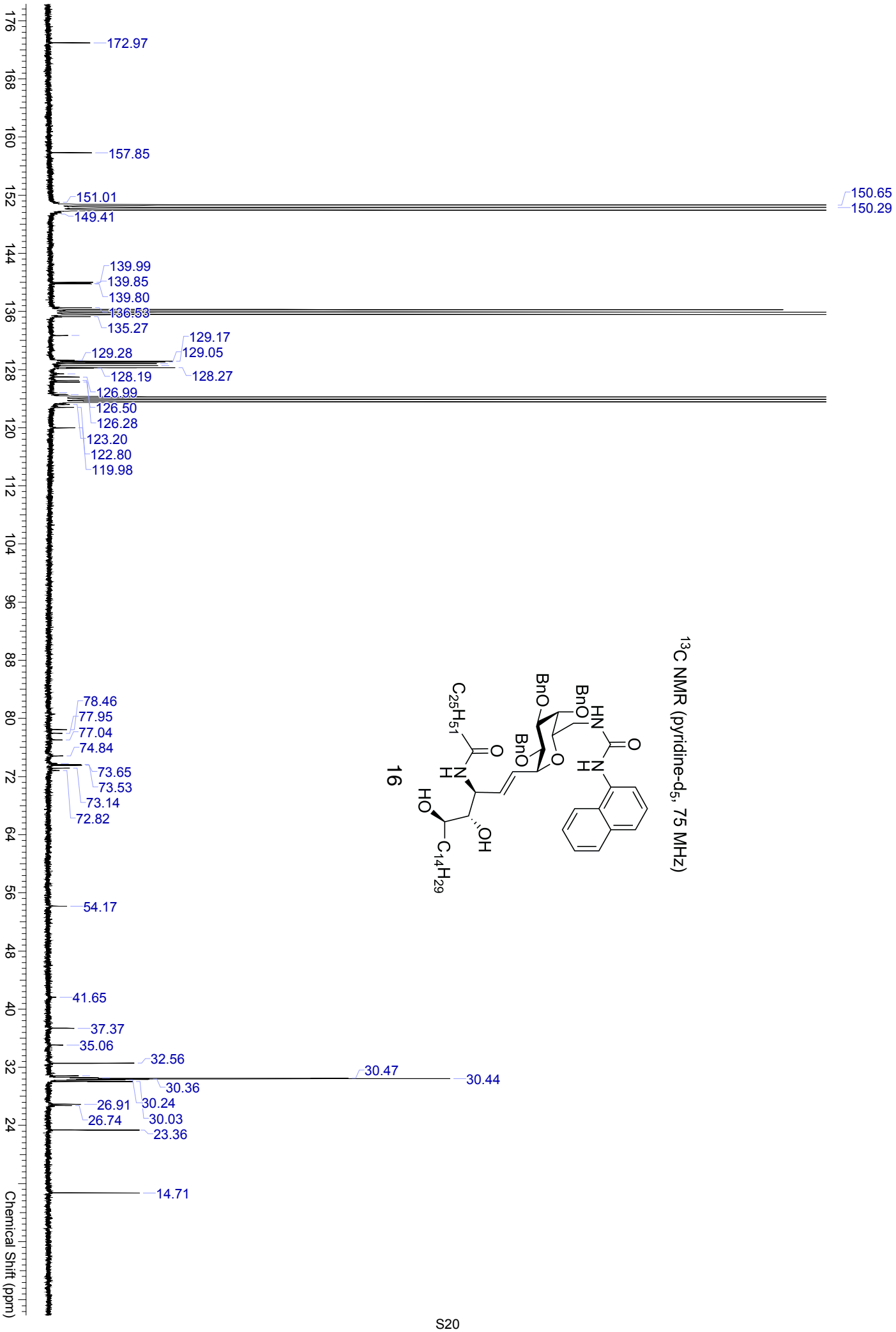
176
168
160
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144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
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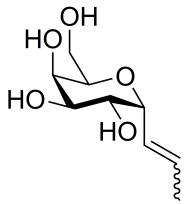
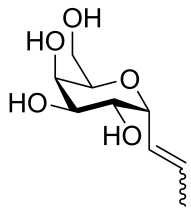
Chemical Shift (ppm)
172.97
157.85
151.01
149.41
150.65
150.29
139.99
139.85
139.80
136.53
135.27
129.28
129.17
129.05
128.27
128.19
126.99
126.50
126.28
123.20
122.80
119.98
78.46
77.95
77.04
74.84
73.65
73.53
73.14
72.82
54.17
41.65
37.37
35.06
32.56
30.47
30.44
30.36
30.24
30.03
26.91
26.74
23.36
14.71
16
^{13}C NMR (pyridine-d$_5$, 75 MHz)

^{1}H NMR (methanol-d_4, 300 MHz)



19

^{13}C NMR (methanol-d_4, 75 MHz)

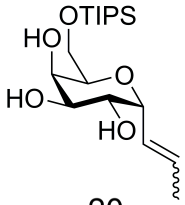


19

132.13
125.44
76.96
73.56
72.06
70.67
69.73
62.57
18.57

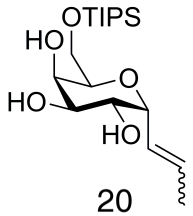
144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 Chemical Shift (ppm)

^{1}H NMR ($CDCl_3$, 300 MHz)

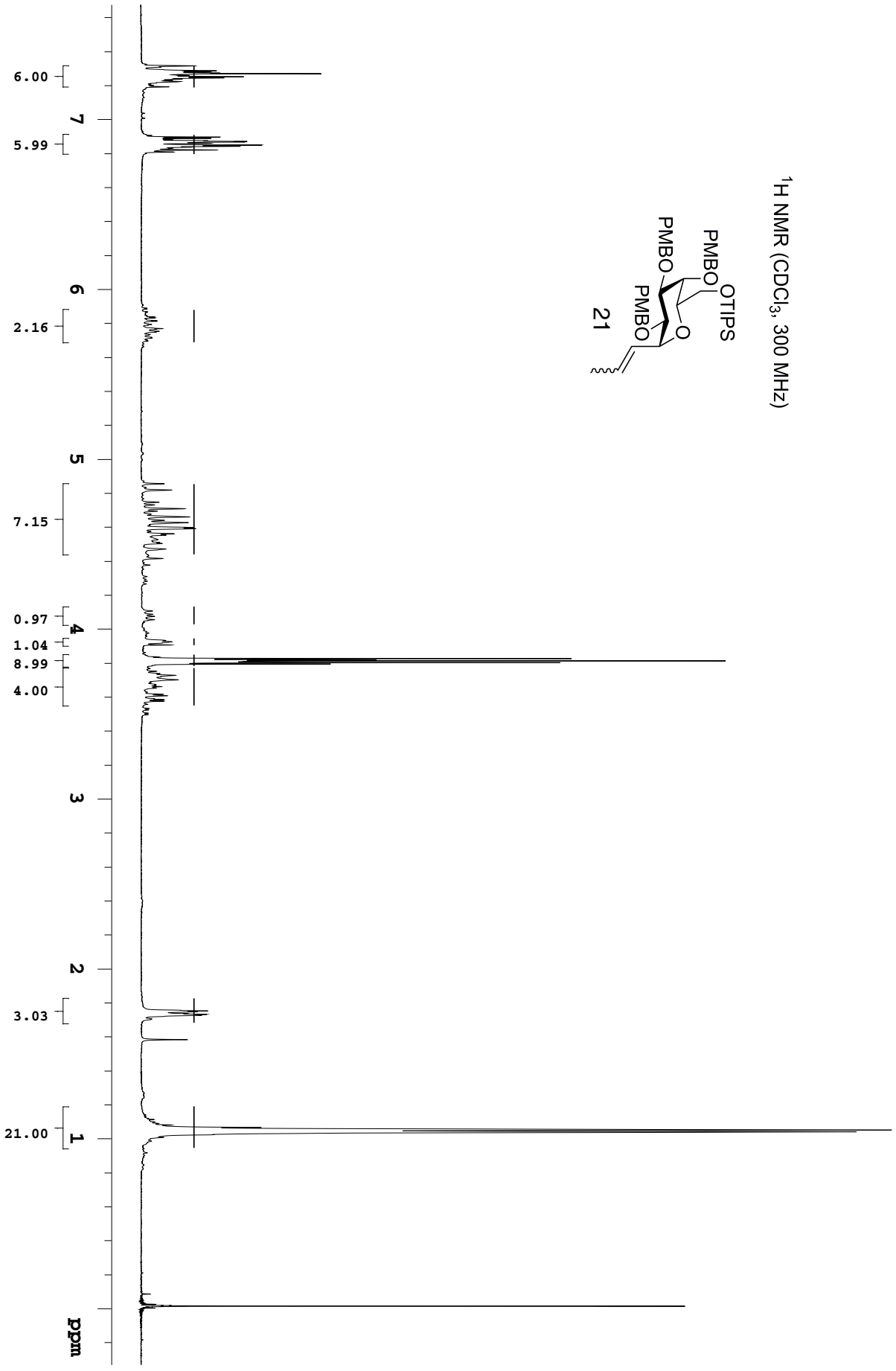


20

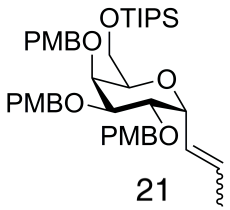
^{13}C NMR ($CDCl_3$, 75 MHz)



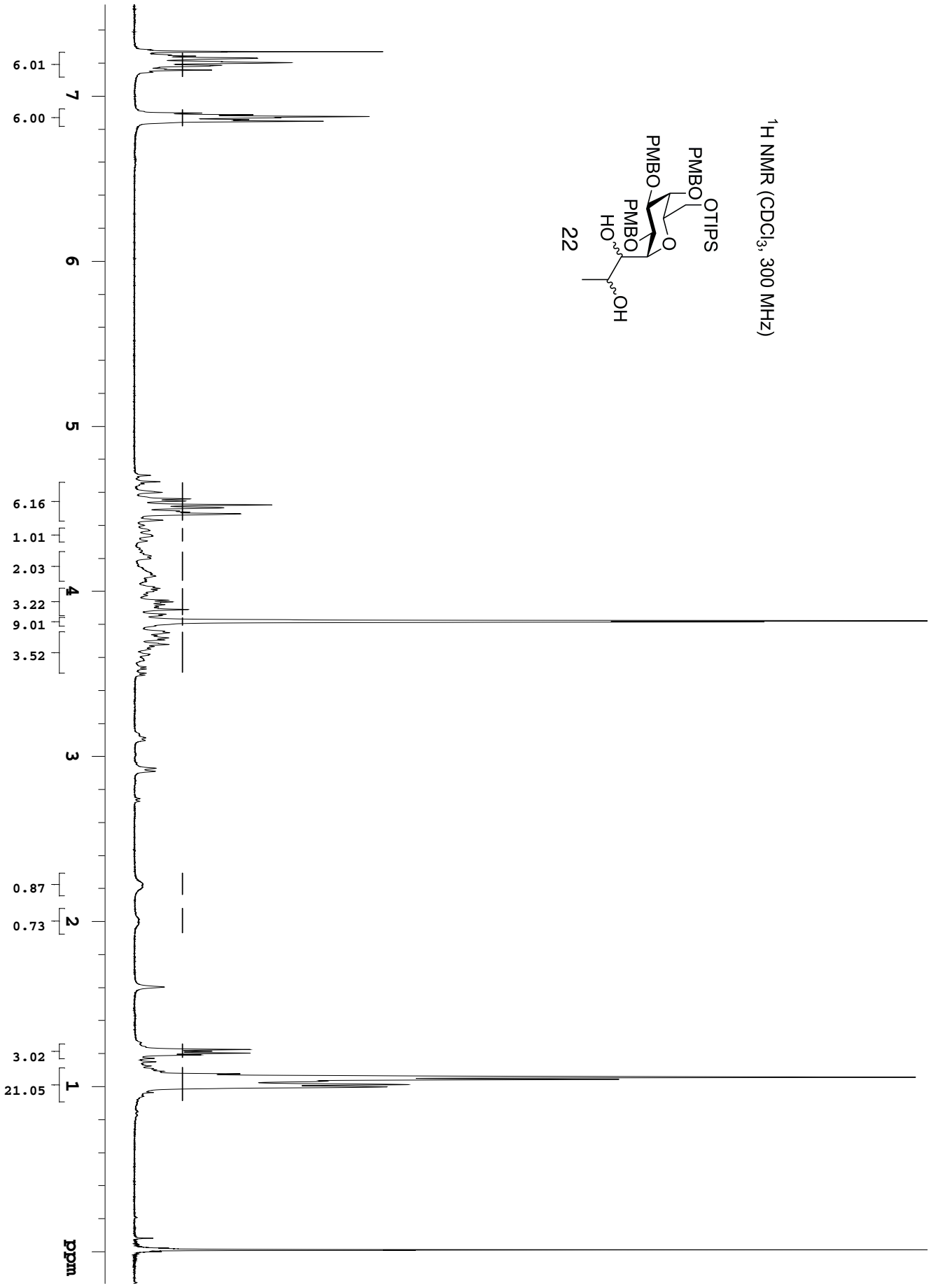
20

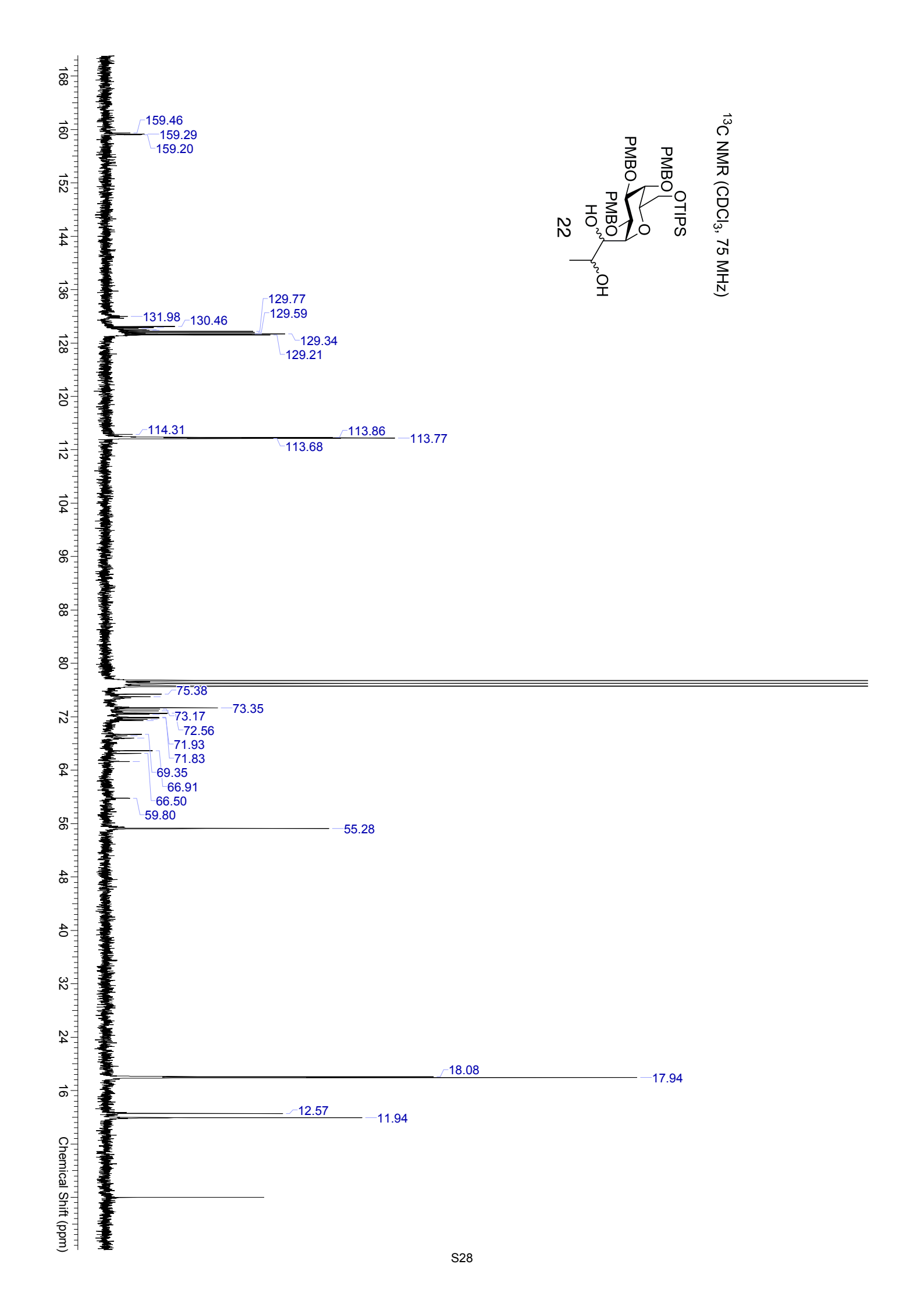

^{1}H NMR ($CDCl_3$, 300 MHz)
21
PMBO
PMBO
PMBO
OTIPS
O
6.00
5.99
2.16
7.15
0.97
1.04
8.99
4.00
3.03
21.00
7
6
5
4
3
2
1
ppm

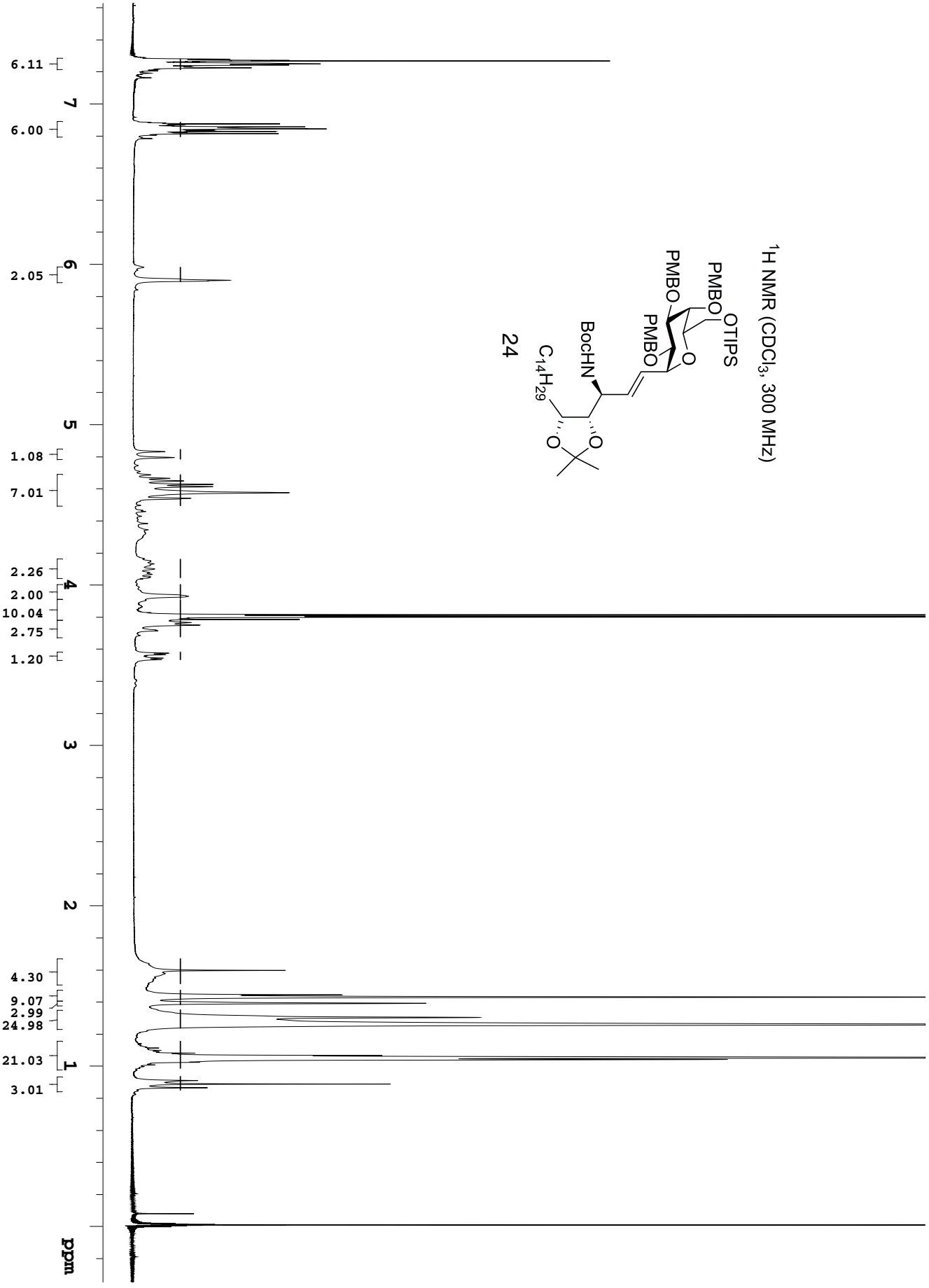
^{13}C NMR ($CDCl_3$, 75 MHz)

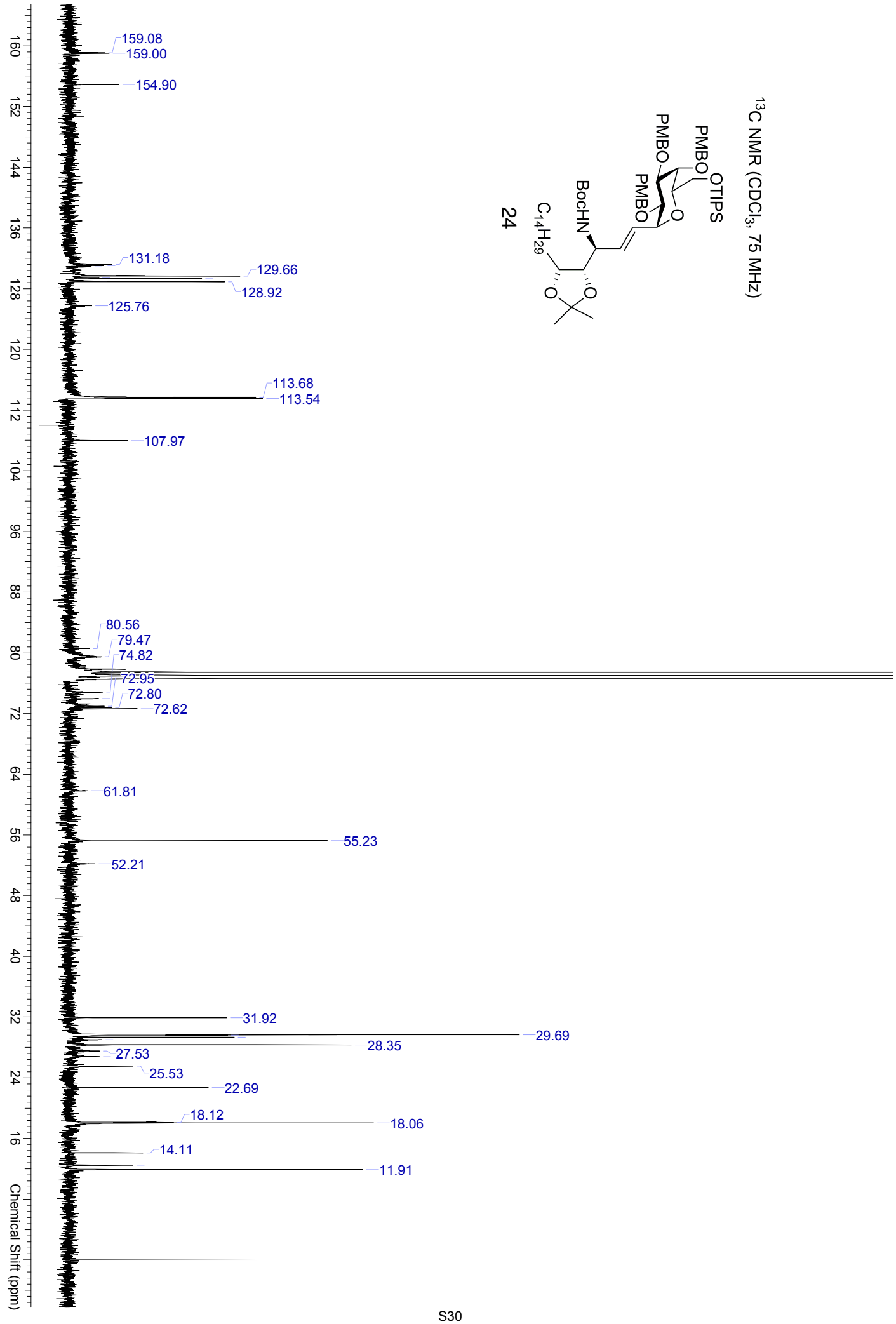


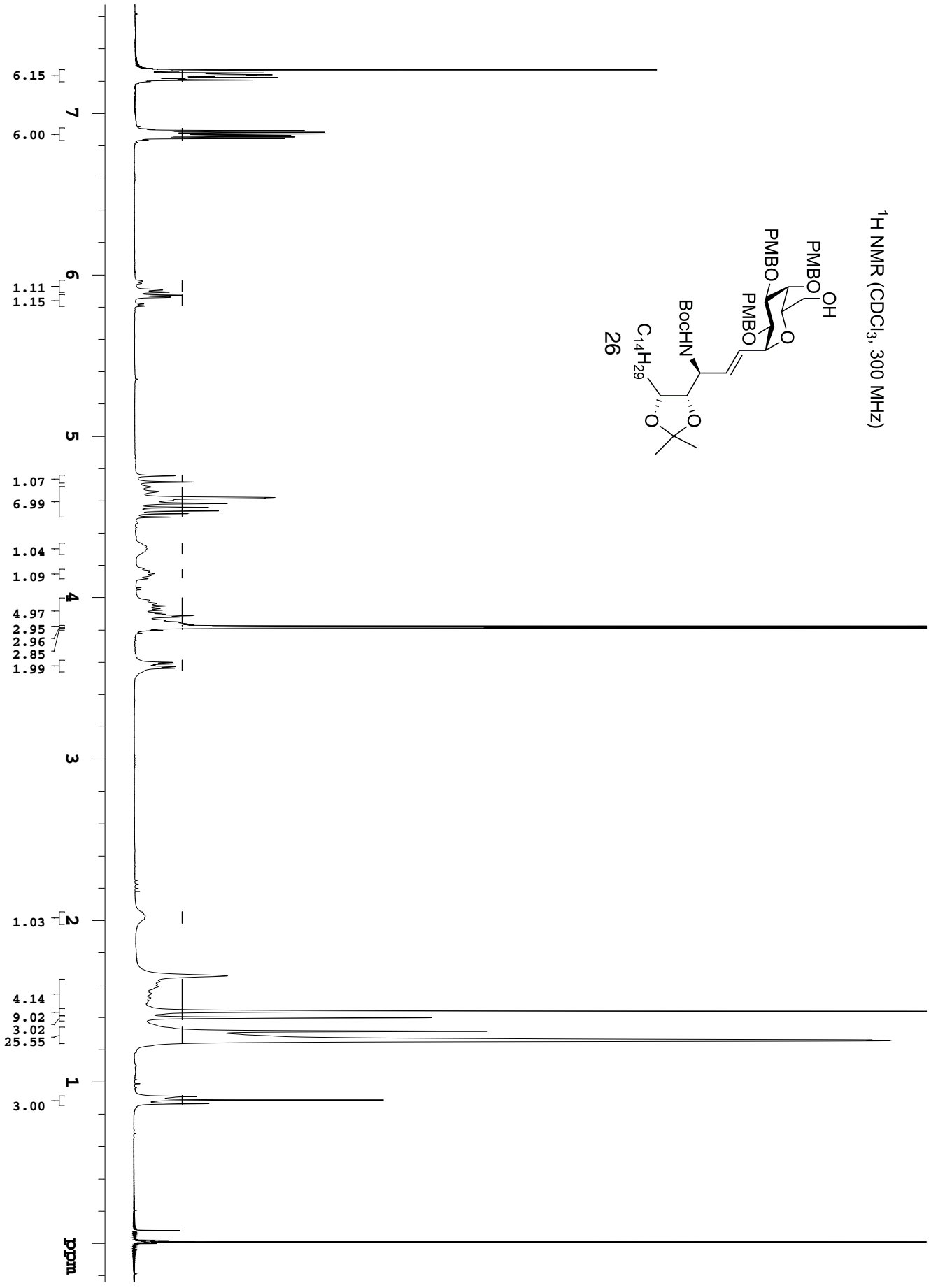
21

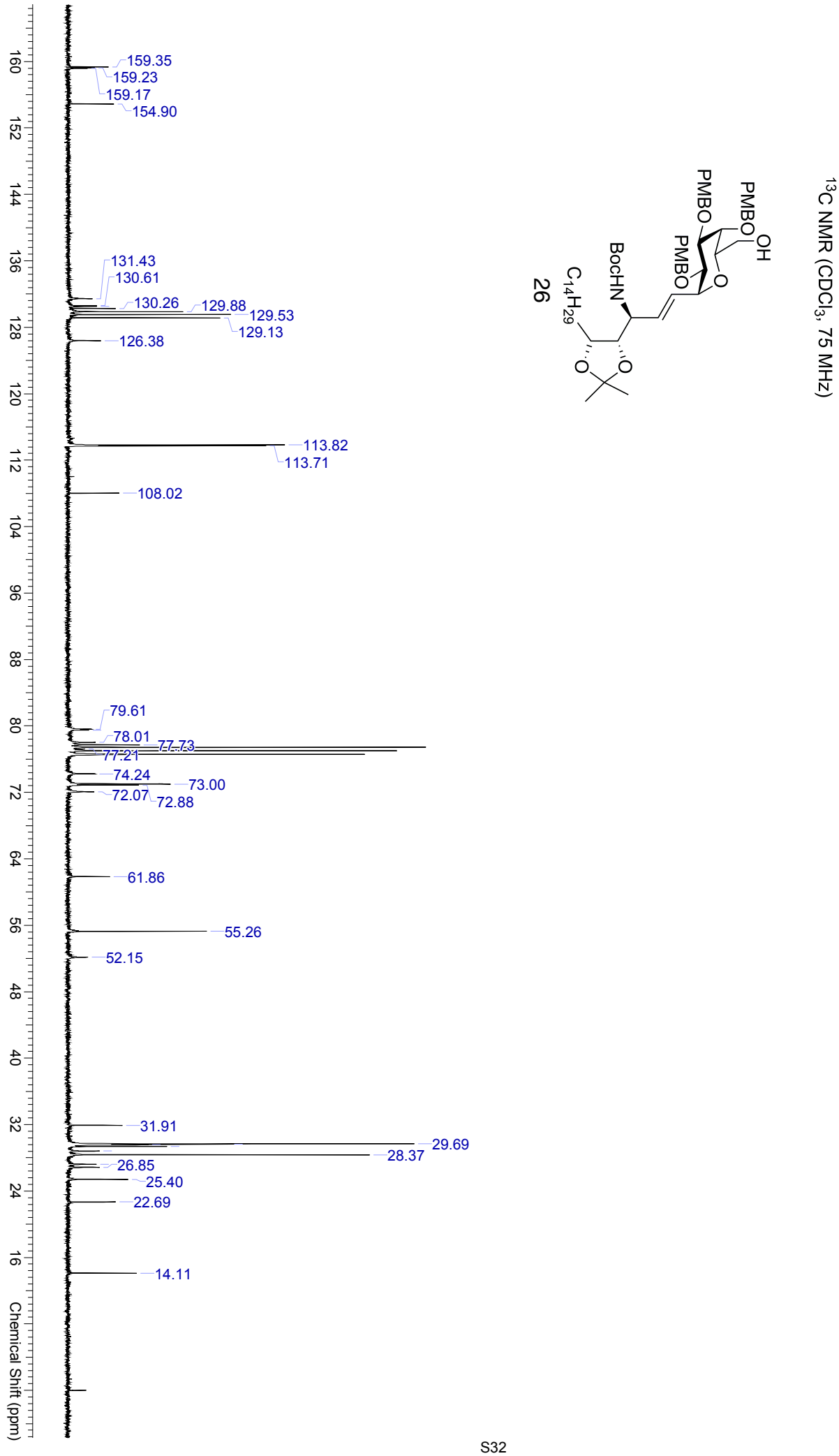

^{1}H NMR ($CDCl_3$, 300 MHz)
22
PMBO
PMBO
PMBO
HO
OTIPS
O
OH
6.01
6.00
6.16
1.01
2.03
3.22
9.01
3.52
0.87
0.73
3.02
21.05
7
6
5
4
3
2
1
ppm

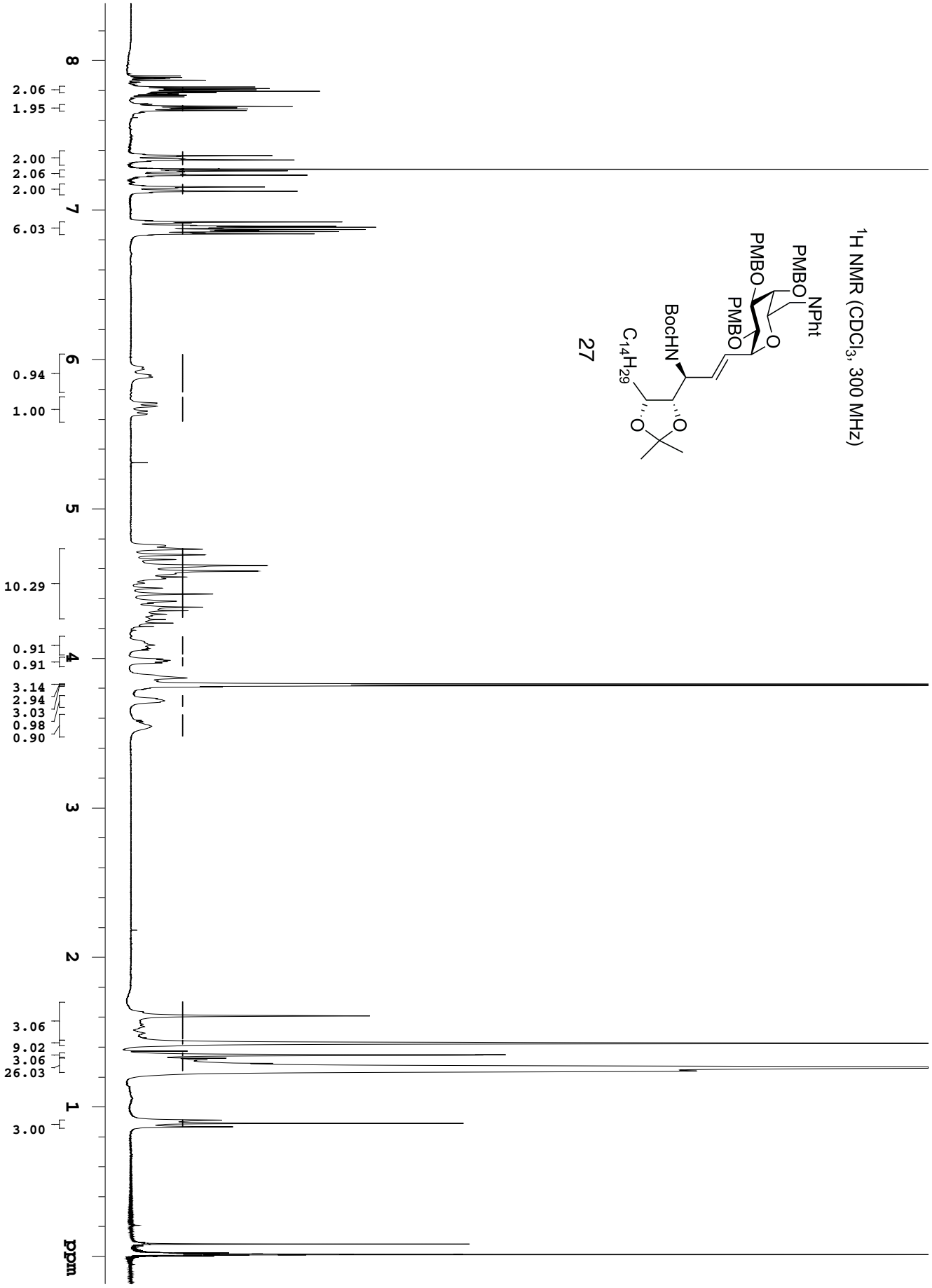

^{13}C NMR ($CDCl_3$, 75 MHz)
PMBO
PMBO
OTIPS
PMBO
HO
O
OH
22
159.46
159.29
159.20
131.98
130.46
129.77
129.59
129.34
129.21
114.31
113.86
113.77
113.68
75.38
73.35
73.17
72.56
71.93
71.83
69.35
66.91
66.50
59.80
55.28
18.08
17.94
12.57
11.94
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


^{1}H NMR (CDCl$_3$, 300 MHz)
24
BocHN
$C_{14}H_{29}$
PMBO
PMBO
PMBO
OTIPS
O
O
O
6.11
6.00
2.05
1.08
7.01
2.26
2.00
10.04
2.75
1.20
4.30
9.07
2.99
24.98
21.03
3.01
7
6
5
4
3
2
1
ppm

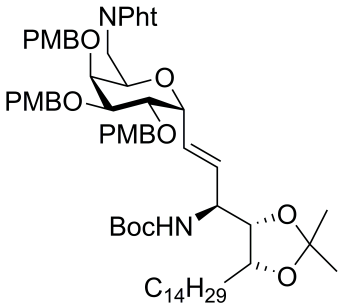

159.08
159.00
154.90
131.18
129.66
128.92
125.76
113.68
113.54
107.97
80.56
79.47
74.82
72.95
72.80
72.62
61.81
55.23
52.21
31.92
29.69
28.35
27.53
25.53
22.69
18.12
18.06
14.11
11.91
Chemical Shift (ppm)
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
24
$C_{14}H_{29}$
BocHN
PMBO
PMBO
PMBO
OTIPS
O
O
O
^{13}C NMR ($CDCl_3$, 75 MHz)


^{1}H NMR ($CDCl_3$, 300 MHz)
26
PMBO
PMBO
PMBO
OH
O
BocHN
$C_{14}H_{29}$
O
O
6.15
6.00
1.11
1.15
1.07
6.99
1.04
1.09
4.97
2.95
2.96
2.85
1.99
1.03
4.14
9.02
3.02
25.55
3.00
7
6
5
4
3
2
1
ppm

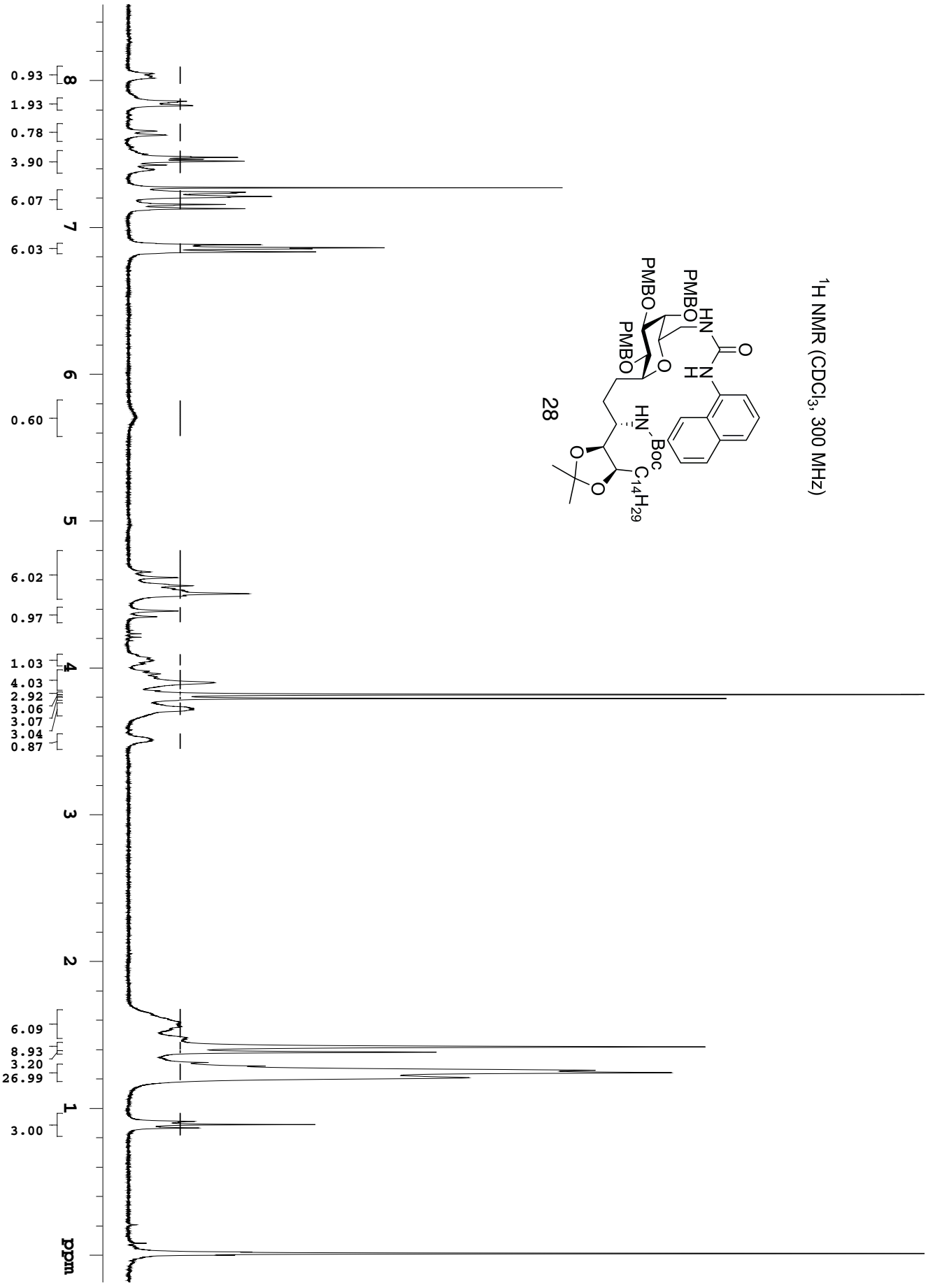

159.35
159.23
159.17
154.90
131.43
130.61
130.26
129.88
129.53
129.13
126.38
113.82
113.71
108.02
79.61
78.01
77.73
77.21
74.24
73.00
72.07
72.88
61.86
55.26
52.15
31.91
29.69
28.37
26.85
25.40
22.69
14.11
Chemical Shift (ppm)
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
PMBO
PMBO
OH
PMBO
O
BocHN
$C_{14}H_{29}$
O
O
26
^{13}C NMR ($CDCl_3$, 75 MHz)


^{1}H NMR (CDCl$_3$, 300 MHz)
27
PMBO
PMBO
PMBO
NPht
O
BocHN
$C_{14}H_{29}$
O
O
8
7
6
5
4
3
2
1
ppm
2.06
1.95
2.00
2.06
2.00
6.03
0.94
1.00
10.29
0.91
0.91
3.14
2.94
3.03
0.98
0.90
3.06
9.02
3.06
26.03
3.00

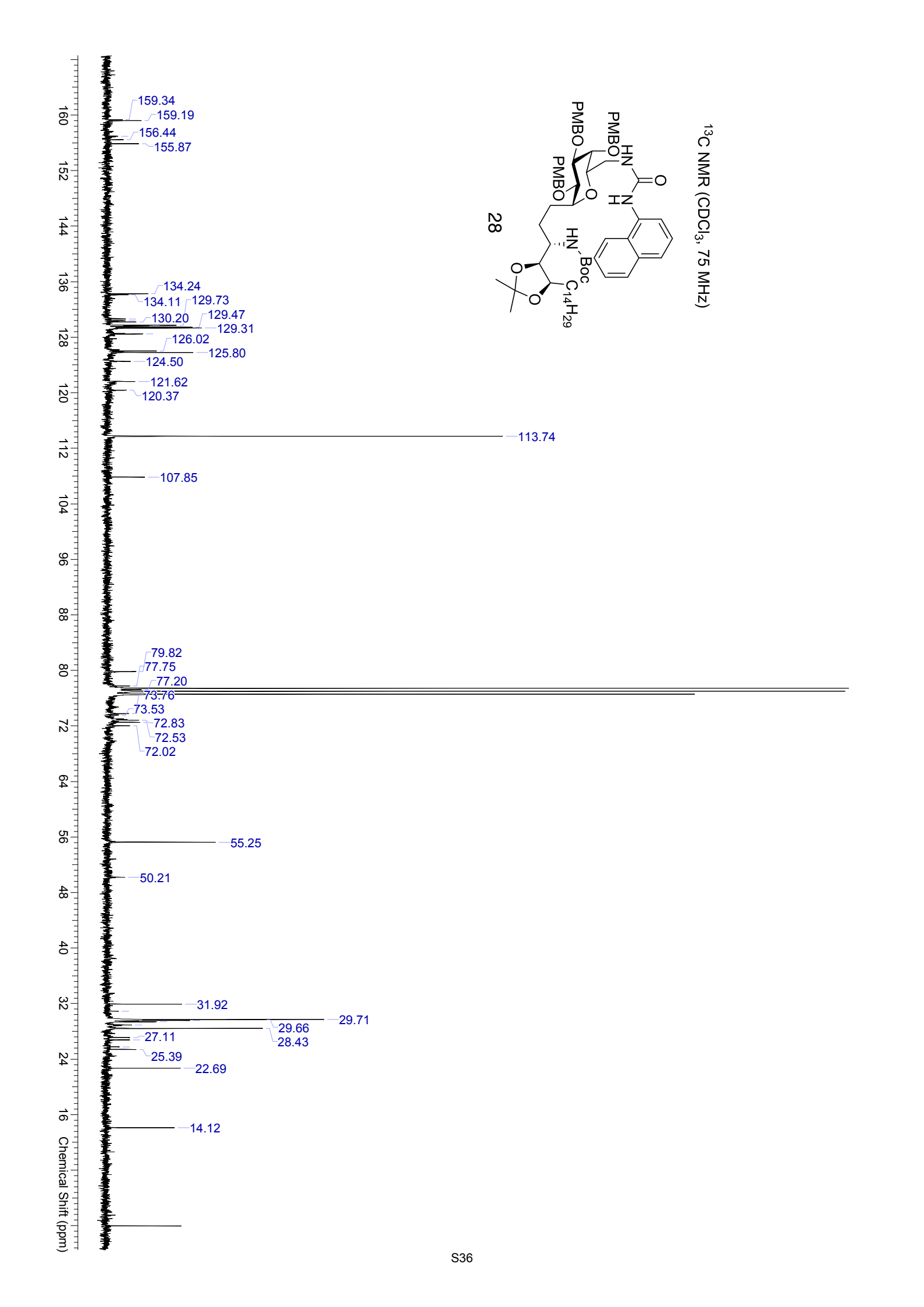
^{13}C NMR ($CDCl_3$, 75 MHz)

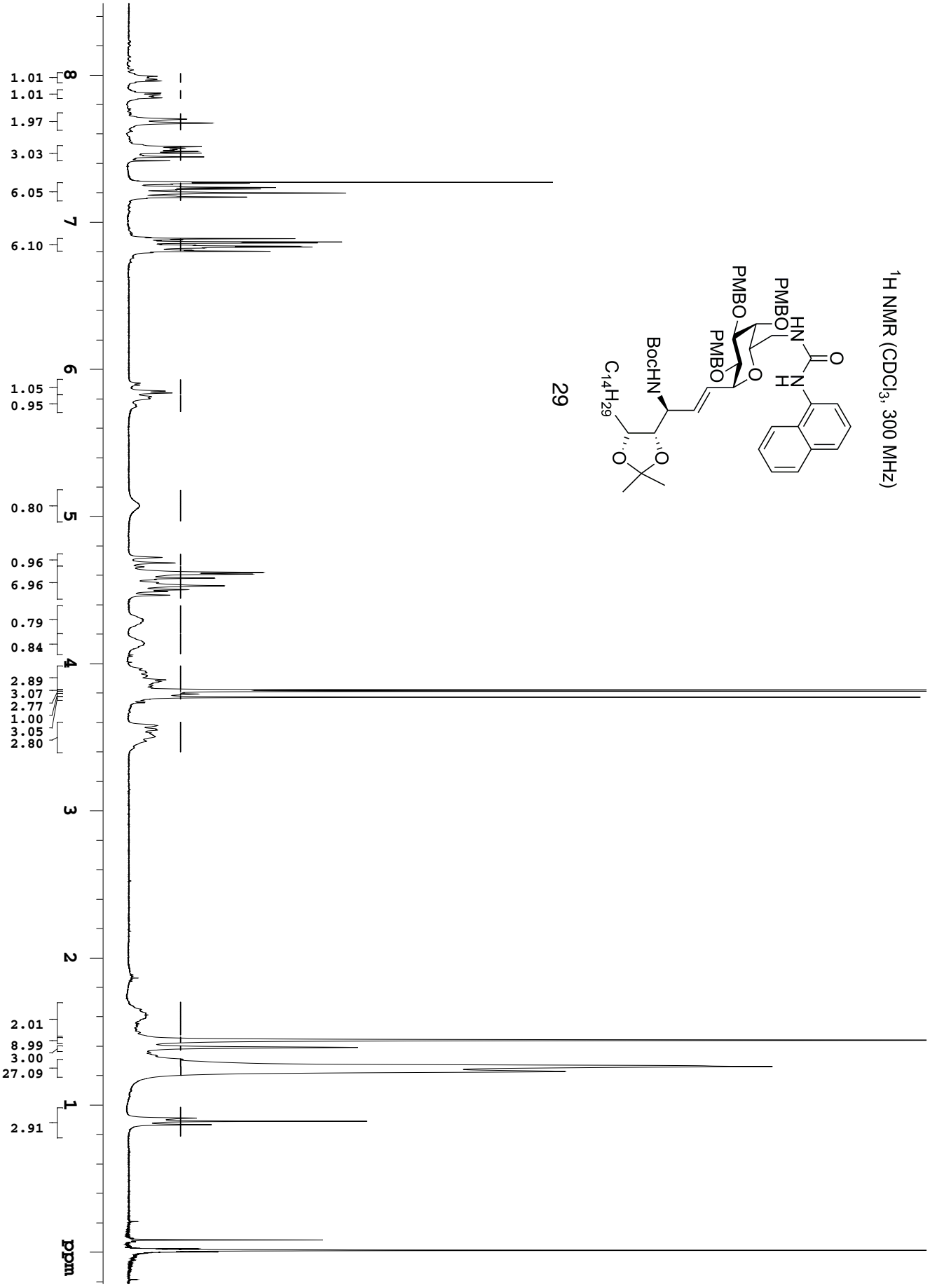


27

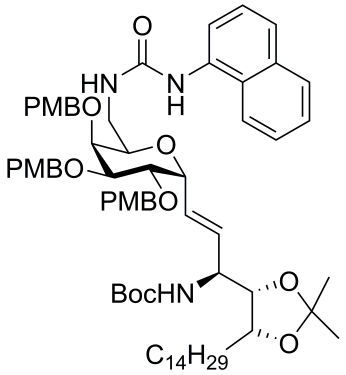


^{1}H NMR ($CDCl_3$, 300 MHz)

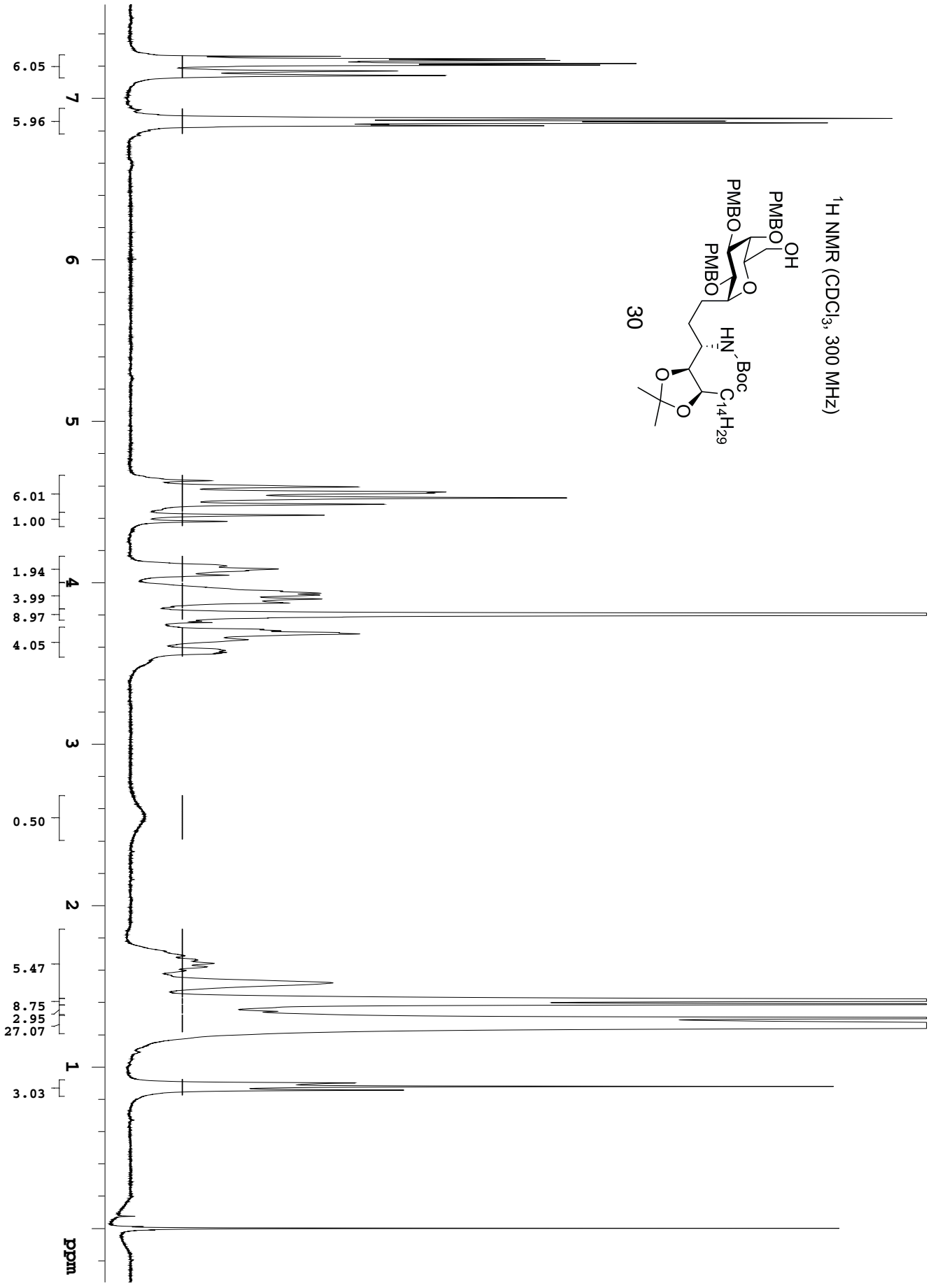

^{13}C NMR (CDCl$_3$, 75 MHz)
28
PMBO
PMBO
PMBO
HN
O
N
H
O
HN
Boc
C$_{14}$H$_{29}$
O
O
159.34
159.19
156.44
155.87
134.24
134.11
129.73
130.20
129.47
129.31
126.02
125.80
124.50
121.62
120.37
113.74
107.85
79.82
77.75
77.20
73.76
73.53
72.83
72.53
72.02
55.25
50.21
31.92
29.71
29.66
28.43
27.11
25.39
22.69
14.12
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


1H NMR (CDCl3, 300 MHz)
29
BocHN
C14H29
PMBO
PMBO
PMBO
HN
H
N
O
O
O
O
O
1.01
1.01
1.97
3.03
6.05
6.10
1.05
0.95
0.80
0.96
6.96
0.79
0.84
2.89
3.07
2.77
1.00
3.05
2.80
2.01
8.99
3.00
27.09
2.91
8
7
6
5
4
3
2
1
ppm

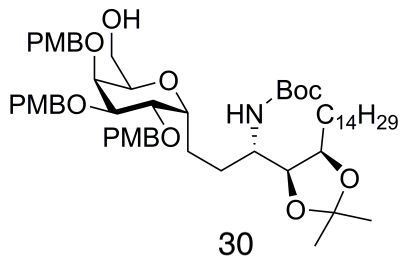
^{13}C NMR ($CDCl_3$, 75 MHz)



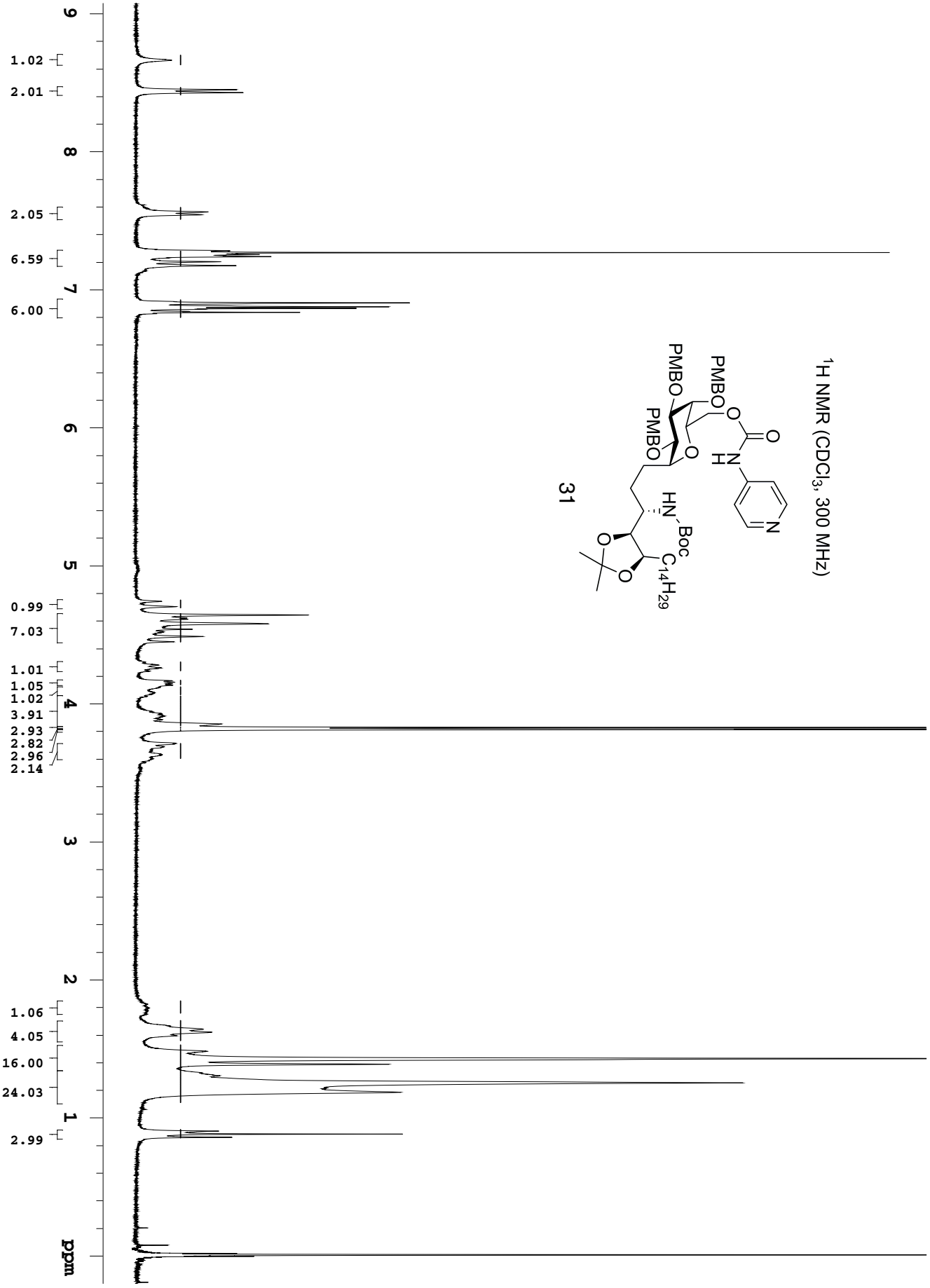
29


^{1}H NMR ($CDCl_3$, 300 MHz)
PMBO
PMBO
PMBO
OH
O
HN
Boc
$C_{14}H_{29}$
O
O
30
6.05
5.96
6.01
1.00
1.94
3.99
8.97
4.05
0.50
5.47
8.75
2.95
27.07
3.03
7
6
5
4
3
2
1
ppm

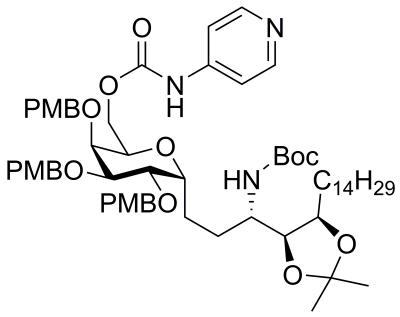
^{13}C NMR ($CDCl_3$, 75 MHz)



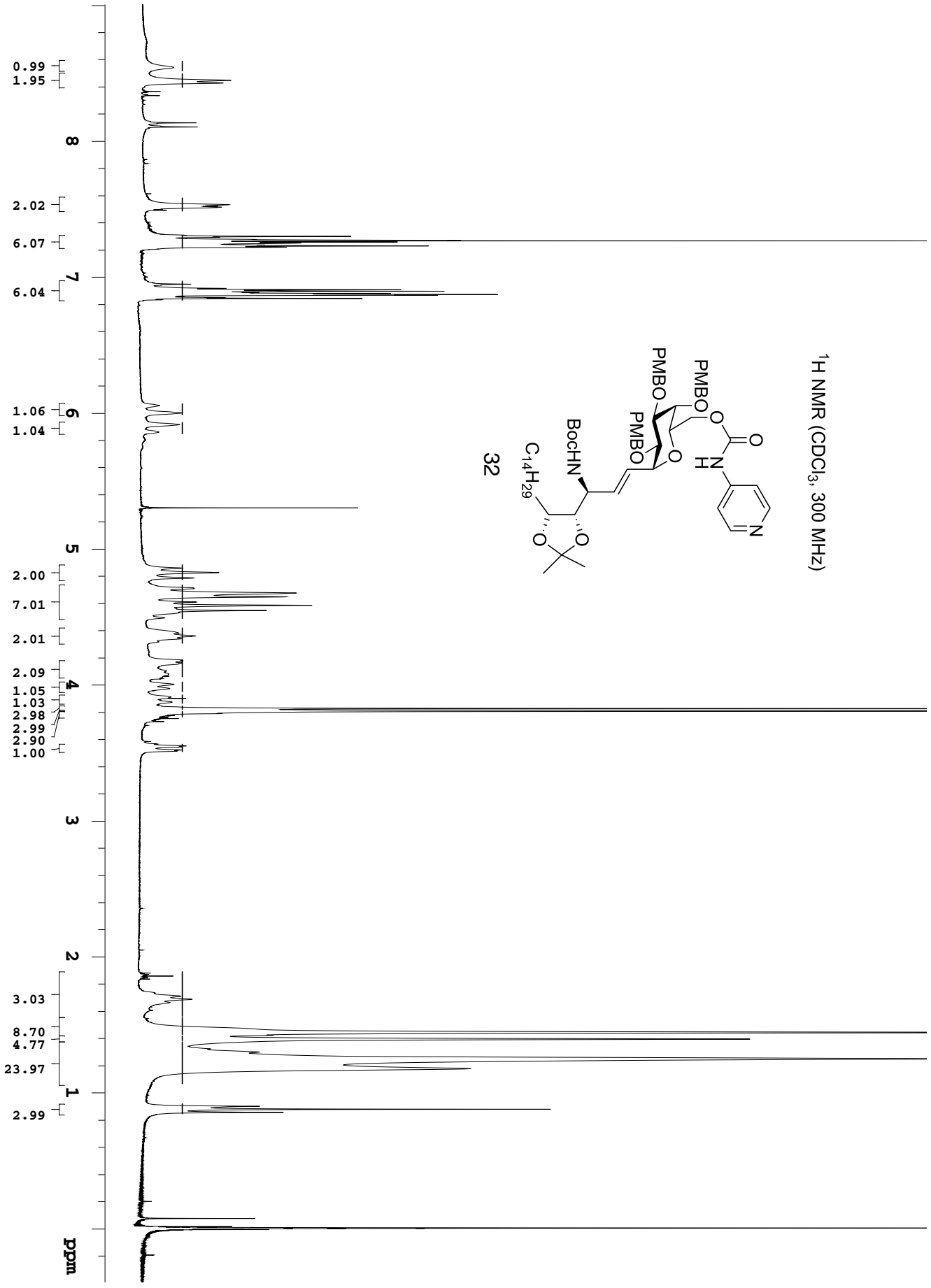
30

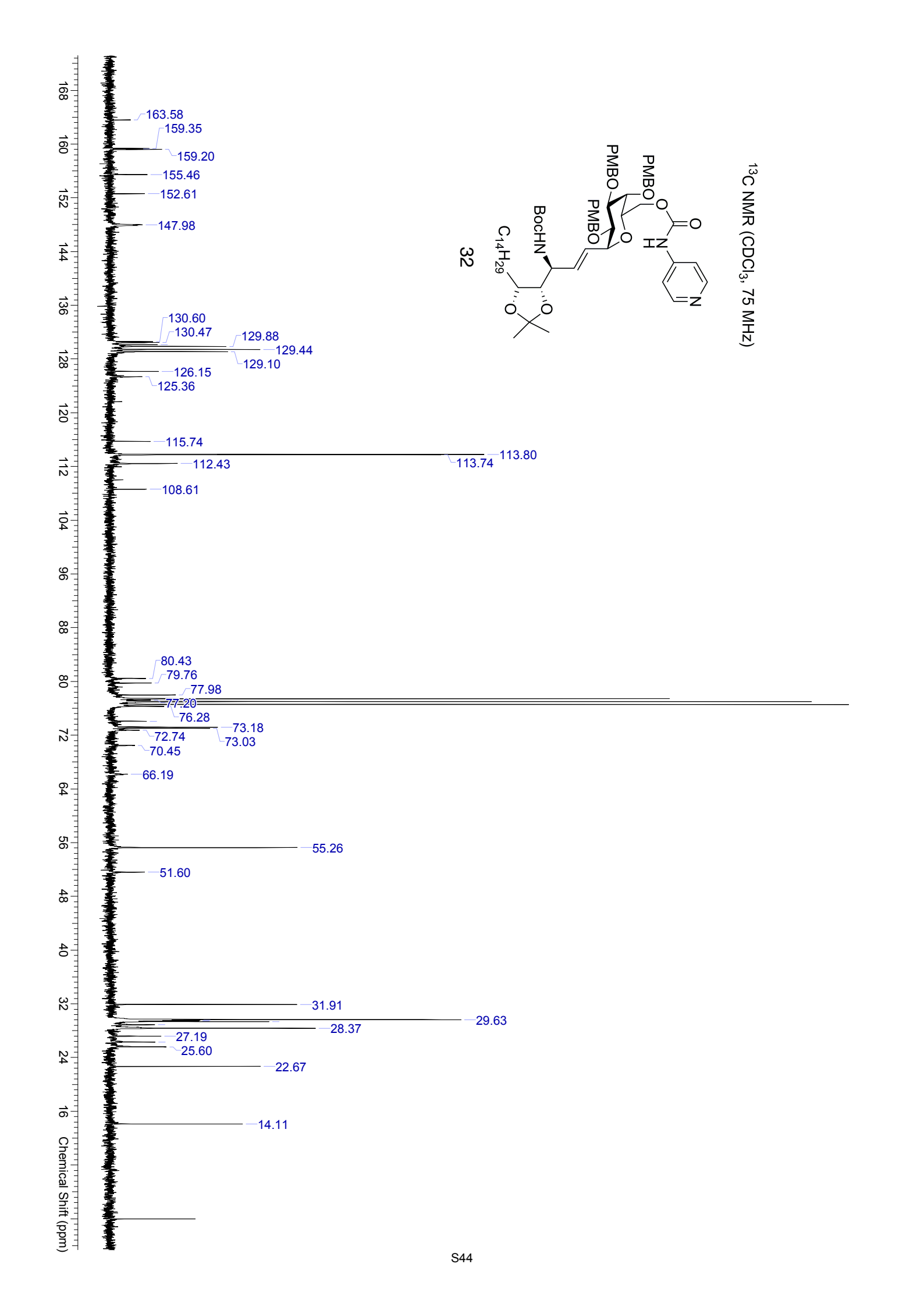

1H NMR (CDCl3, 300 MHz)
31
PMBO
PMBO
PMBO
O
N
H
HN
Boc
C14H29
O
O
N
9
8
7
6
5
4
3
2
1
ppm
1.02
2.01
2.05
6.59
6.00
0.99
7.03
1.01
1.05
1.02
3.91
2.93
2.82
2.96
2.14
1.06
4.05
16.00
24.03
2.99

^{13}C NMR ($CDCl_3$, 75 MHz)

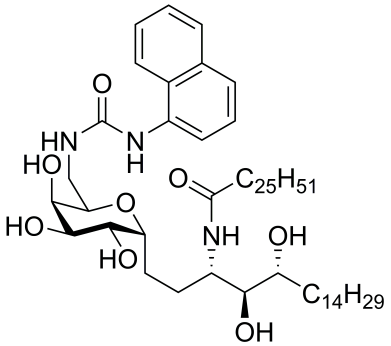


31

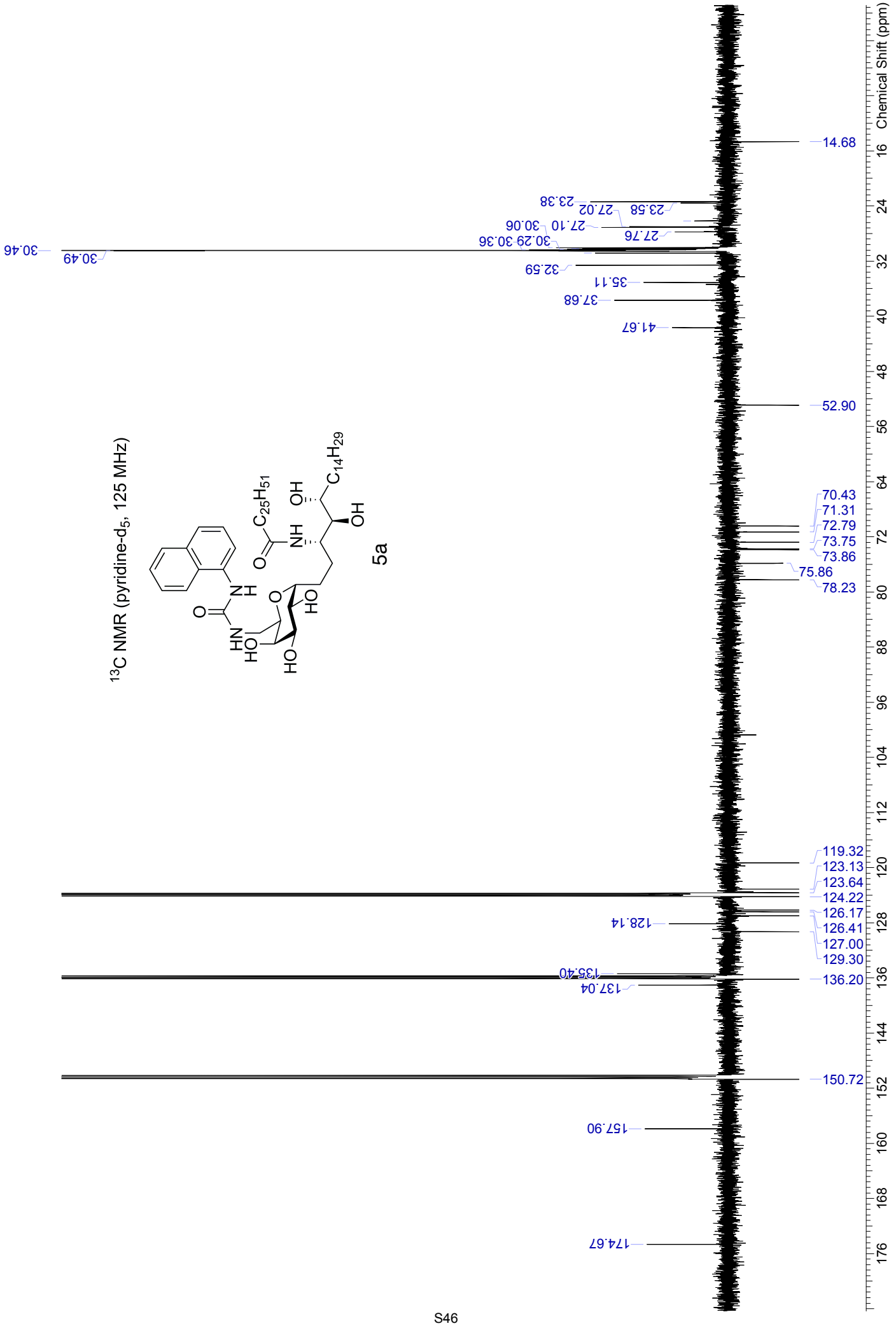

0.99
1.95
2.02
6.07
6.04
1.06
1.04
2.00
7.01
2.01
2.09
1.05
1.03
2.98
2.99
2.90
1.00
3.03
8.70
4.77
23.97
2.99
8
7
6
5
4
3
2
1
ppm
PMBO
PMBO
PMBO
O
O
O
O
H
N
N
BocHN
$C_{14}H_{29}$
32
^{1}H NMR ($CDCl_3$, 300 MHz)

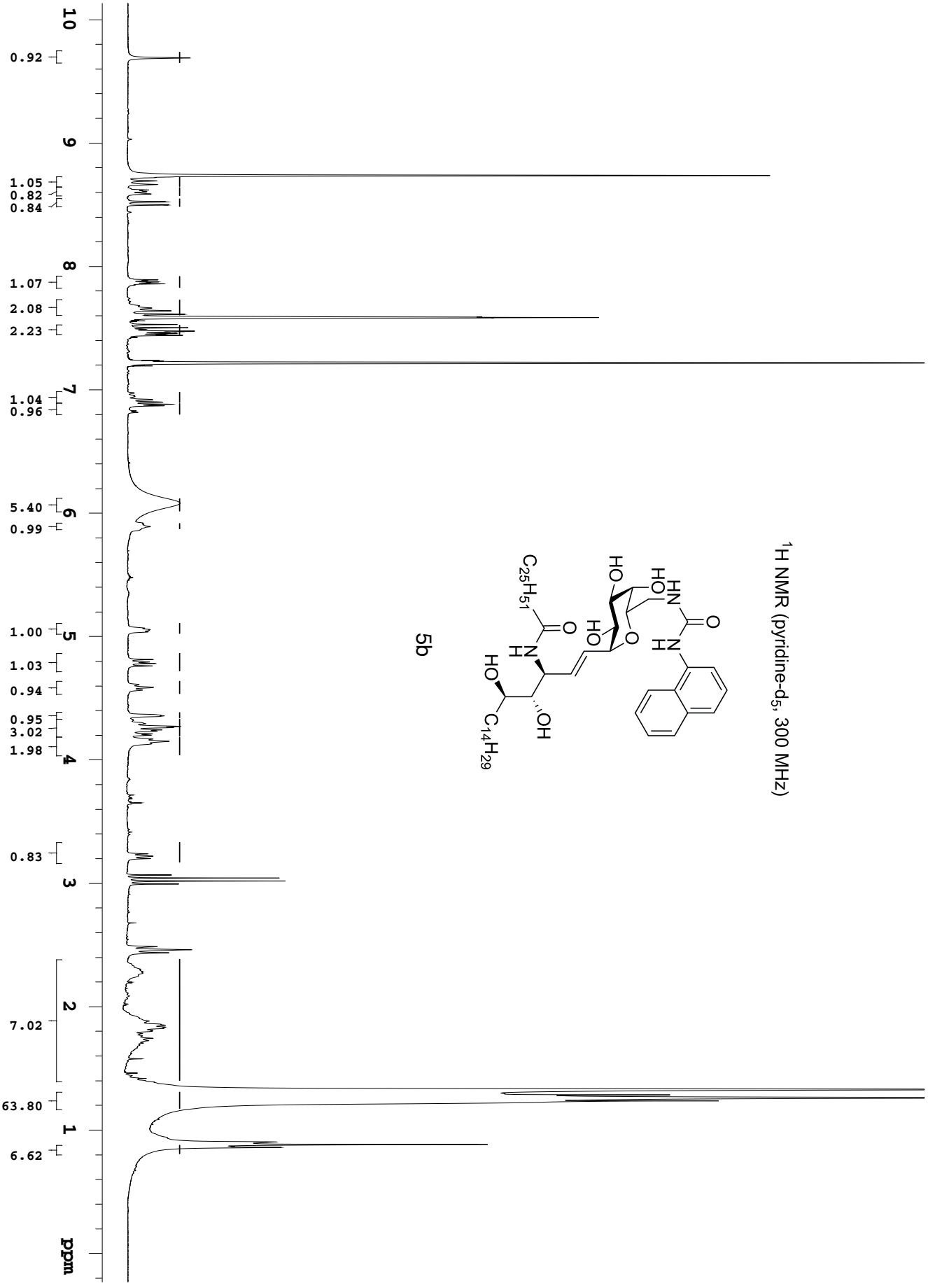

^{13}C NMR (CDCl$_3$, 75 MHz)
32
PMBO
PMBO
PMBO
BocHN
$C_{14}H_{29}$
O
O
O
O
O
O
N
H
N
163.58
159.35
159.20
155.46
152.61
147.98
130.60
130.47
129.88
129.44
129.10
126.15
125.36
115.74
113.80
113.74
112.43
108.61
80.43
79.76
77.98
77.20
76.28
73.18
73.03
72.74
70.45
66.19
55.26
51.60
31.91
29.63
28.37
27.19
25.60
22.67
14.11
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)

^{1}H NMR (pyridine-d_5, 500 MHz)



5a

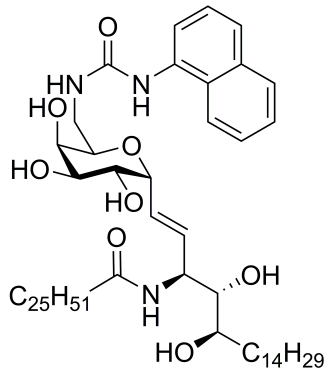

^{13}C NMR (pyridine-d$_5$, 125 MHz)
5a
Chemical Shift (ppm)
14.68
23.38
23.58
27.02
27.10
27.76
30.06
30.29
30.36
30.46
30.49
32.59
35.11
37.68
41.67
52.90
70.43
71.31
72.79
73.75
73.86
75.86
78.23
119.32
123.13
123.64
124.22
126.17
126.41
127.00
128.14
129.30
135.40
136.20
137.04
150.72
157.90
174.67



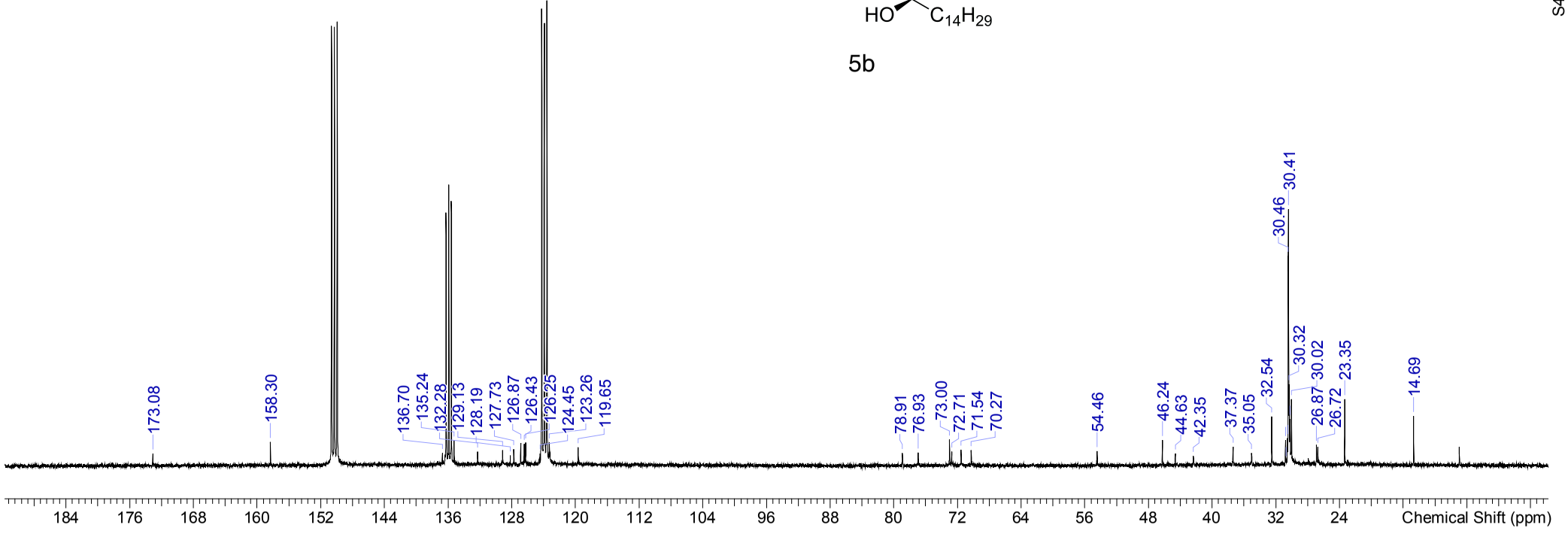
5b

^{1}H NMR (pyridine-d_5, 300 MHz)

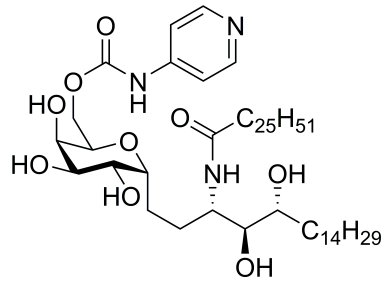
^{13}C NMR (pyridine-d$_5$, 75 MHz)



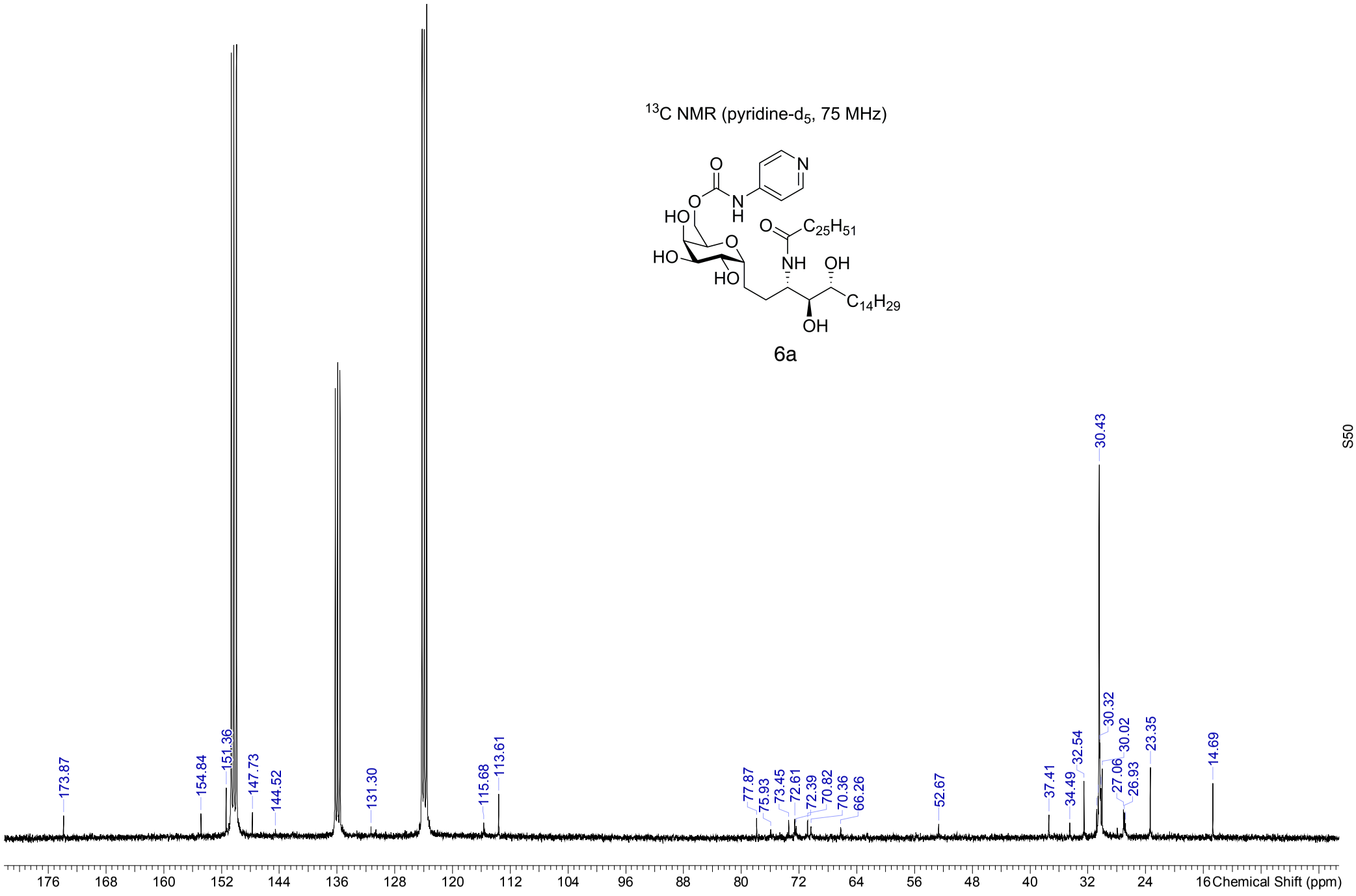
5b

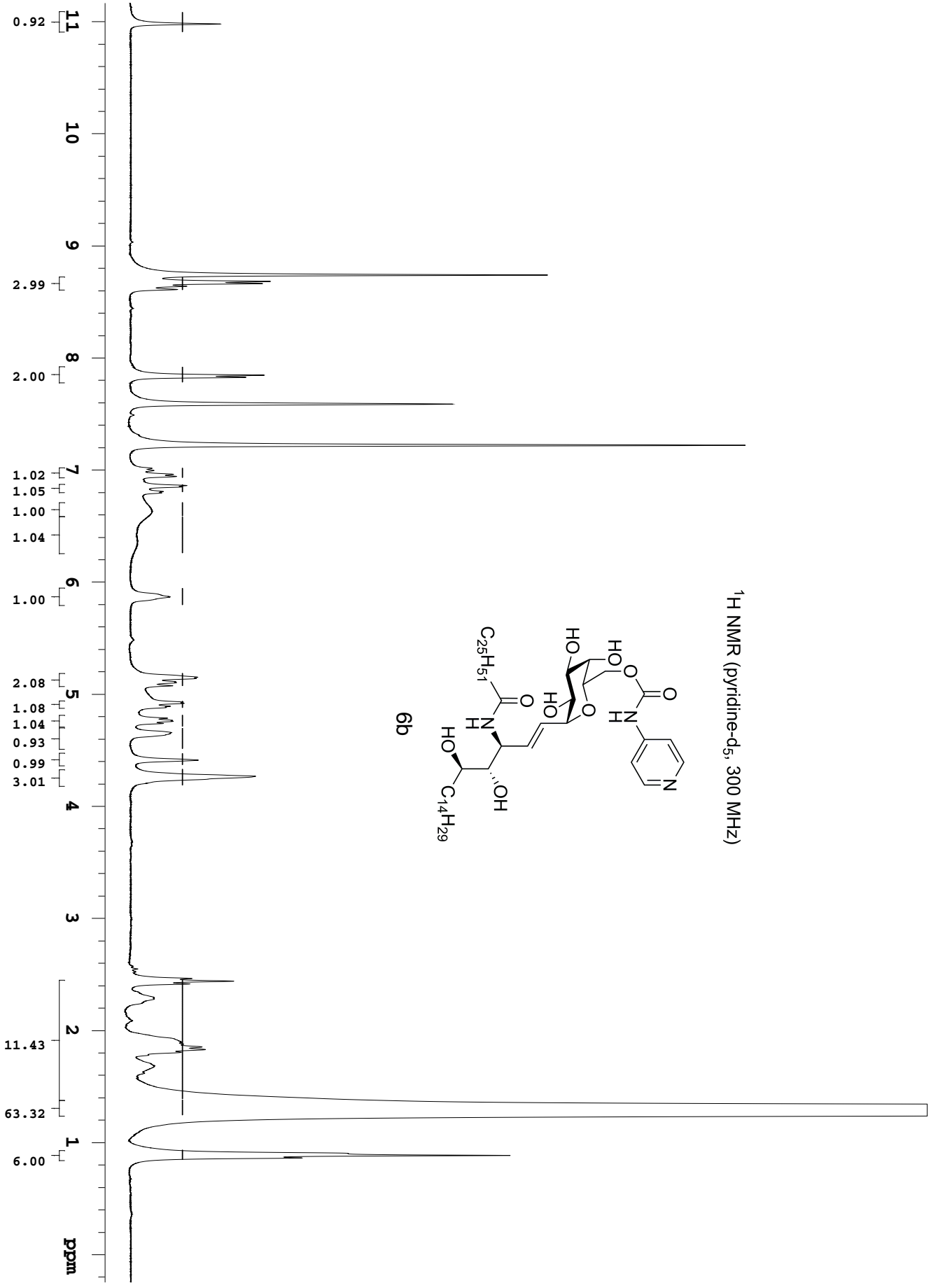


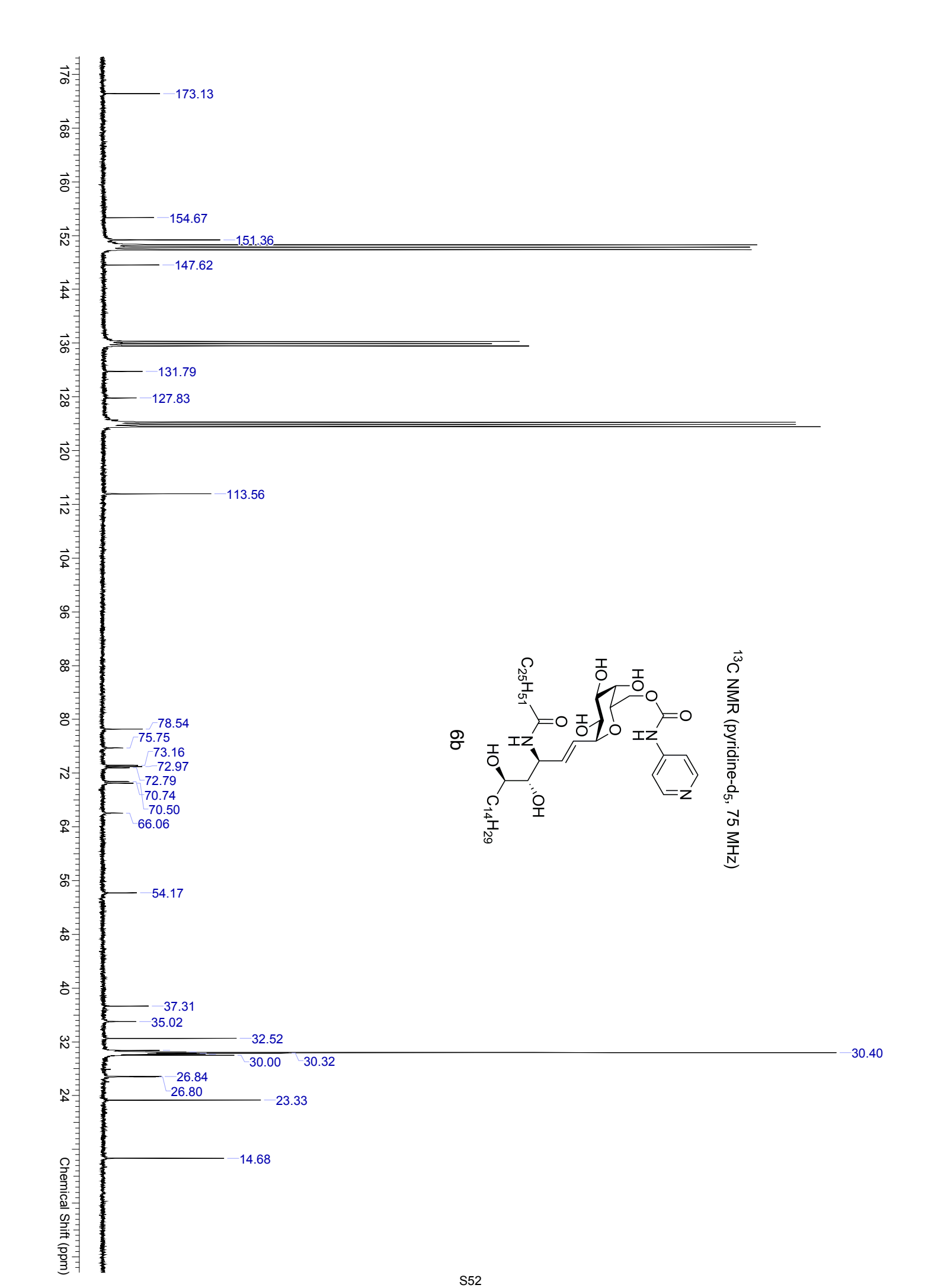
^{1}H NMR (pyridine-d_5, 300 MHz)



6a


^{13}C NMR (pyridine-d$_5$, 75 MHz)
6a
173.87
154.84
151.36
147.73
144.52
131.30
115.68
113.61
77.87
75.93
73.45
72.61
72.39
70.82
70.36
66.26
52.67
37.41
34.49
32.54
30.43
30.32
30.02
27.06
26.93
23.35
14.69
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


0.92
2.99
2.00
1.02
1.05
1.00
1.04
1.00
2.08
1.08
1.04
0.93
0.99
3.01
11.43
63.32
6.00
11
10
9
8
7
6
5
4
3
2
1
ppm
6b
^{1}H NMR (pyridine-d$_5$, 300 MHz)


^{13}C NMR (pyridine-d$_5$, 75 MHz)
6b
C$_{25}$H$_{51}$
C$_{14}$H$_{29}$
HO
OH
O
N
H
Chemical Shift (ppm)
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
173.13
154.67
151.36
147.62
131.79
127.83
113.56
78.54
75.75
73.16
72.97
72.79
70.74
70.50
66.06
54.17
37.31
35.02
32.52
30.40
30.00
30.32
26.84
26.80
23.33
14.68

Supporting figures

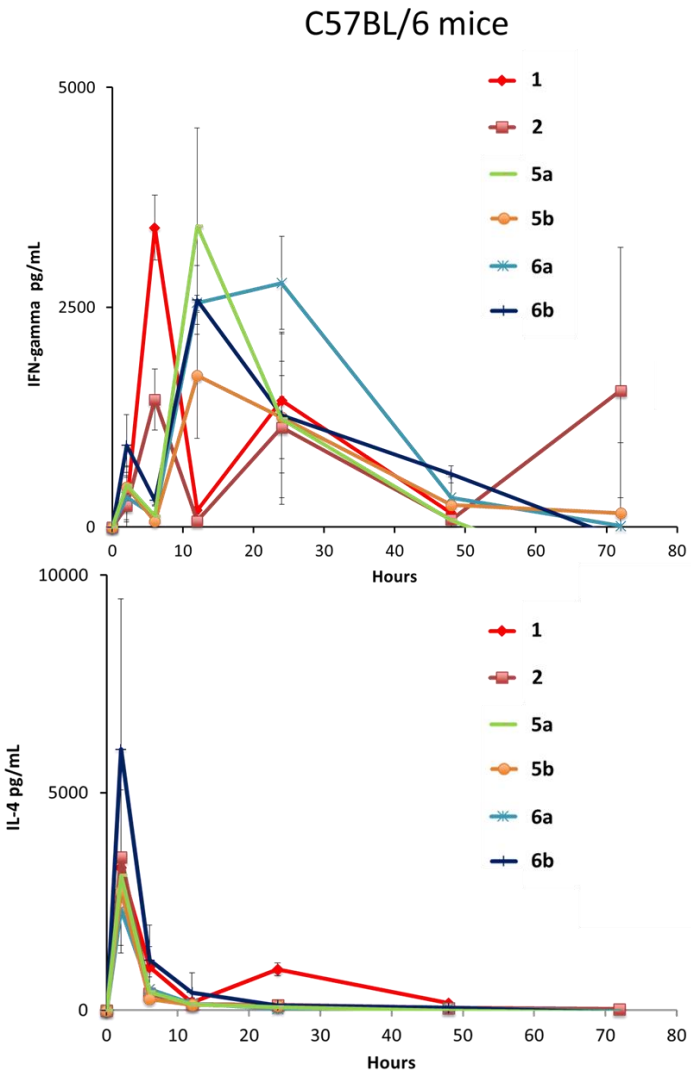


Figure S1: IFN-γ and IL-4 secretion, measured over the course of 72h, after intraperitoneal injection of 1 µg of the final compounds in C57BL/6 mice

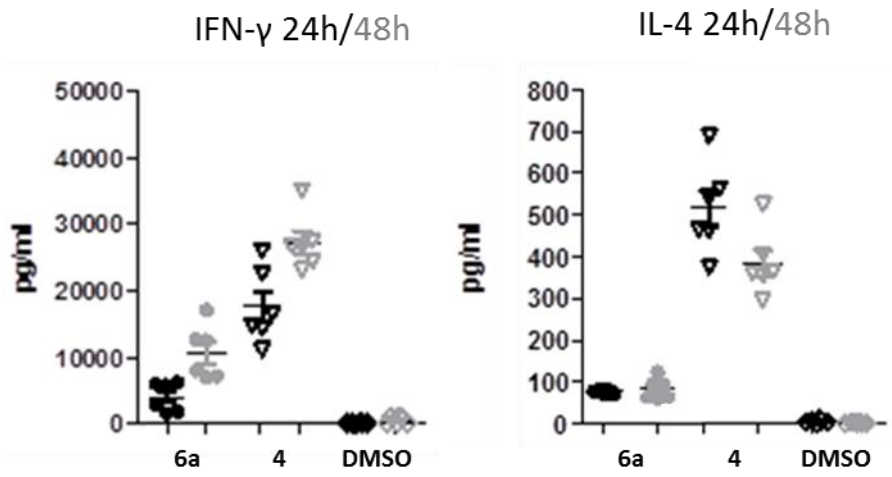


Figure S2: IFN-γ and IL-4 secretion after coculture of human *i*NKT cells and PBMC's incubated overnight with 100 ng/mL of the corresponding glycolipids

Human *i*NKT cultures (figure S2)

Human *i*NKT cells from healthy adult individuals were FACS-sorted and expanded as described previously.[i] Peripheral blood mononuclear cells (PBMC) were isolated by means of density centrifugation and T cell-depleted by negative selection with CD2 Pan T Dynabeads (Dynal). T cell depleted PBMC were incubated overnight in the presence of indicated glycolipids (100 ng/ml) or DMSO and used as lipid antigen presenting cells (APC). Subsequently, $5x10^4$ *i*NKT cells were cocultured with $5x10^4$ glycolipid pulsed APC in RPMI 1640 media supplemented with 10% FBS, 1% sodium pyruvate, 1% nonessential amino acids and 1% penicillin/streptomycin (all from Thermofisher Scientific) and 1U/ml IL-2 (Roche). Supernatants were collected after 24hr and 48hrs of culture and IL-4 and IFN-γ levels were determined by means of ELISA (eBioscience).

[i] Venken, K.; Decruy, T.; Aspeslagh, S.; Van Calenbergh, S.; Lambrecht, B. N.; Elewaut, D. *J. Immunol.* **2013**, 191, 2174.